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MEDICAL SCHOOL

VOLUME IX

ANATOMY, PHYSIOLOGY, PATHOLOGY, BACTERIOLOGY, DICTIONARY

EDITED BY

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ANATOMY AND PATHOLOGY.

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SECTION I

ANATOMY.

Anatomy was the first of the medical sciences to be taught by the laboratory method. The possibilities of training the mind and hand in the teaching of anatomy have always been present in the minds of some instructors. It is known to all those who have watched the evolution of medical pedagogy that the influence of anatomy methods spread first to such secondary sciences as histology, chemistry, bacteriology, etc., and now embraces the clinical branches. In spite of the wider and better ideals of anatomy, many teachers still teach nothing in the dissecting room except some anatomic facts. Many, however, are using the opportunities of their laboratories to teach mental methods, and to train fingers and hands. On the basis of the evident scope of intent of their teaching heads. Mall[1] classifies the medical schools of this country as follows:

1. Those schools in which there are lectures and a dissecting room in which the student dissects undirected and oftentimes unassisted.
2. Those schools in which the didactic work is recitative, closely following some text, and supplemented by a dissecting room in which the student learns enough to pass the State Board and other examinations. This is largely memory training.
3. In this group are those schools in which the student is stimulated to proceed along his own lines, to carefully work out, in text, in lecture, and in dissecting room, the practical anatomic questions which have been suggested by clinical study.
4. In the fourth group the plans of the third group are so extended as to include questions raised in physiology,

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(1) Johns Hopkins Hospital Bulletin, 1905.

neurology, pathology and other sciences, as well as those in the third group.

Mall thinks the anatomic laboratory is an excellent place to teach the student the importance of attention to small things, of doing all things well, of independent observation, of originality of thought and plan, and technical skill.

Nature of the Mammalian Diaphragm and Pleural Cavities. According to the researches of Keith,[1] the abdominal viscera constitute the relatively fixed points in fetal development. The liver and other abdominal organs retain approximately their relations to the umbilicus throughout development. The development of the chest and neck carries the head, throat and lungs a long way from their points of origin. The lungs develop as a bud from the fore gut, and the remnants of the mesentery of that period of development is shown in the attachments between the esophagus and the mediastinal and diaphragmatic structures, the esophagus being the relatively stable structure in this region. In amphibians the lungs are found wholly within the abdomen. In birds they are partly within the abdomen, partly within the thorax; while in man they are wholly within the thorax.

He compares the migration of the lungs to that of the testicle, and the explanation of hernia is the same in the two localities. The element of gravity and of the direction of application of the force of abdominal muscle contraction is a factor in the relative frequency of hernias through the inguinal ring, as compared with those through the pleuro-peritoneal openings. The human diaphragm consists of two muscular portions and one fibrous. The anterior or sterno-costal portion develops from the inner sheath of the rectus muscle; the fibers run generally toward the central tendon. The posterior or spinal portions arise from the quadratus lumborum and psoas.

Keith thinks there is much evidence that the diaphragm is not essentially a respiratory organ, but serves by contraction to compress the liver and other abdominal viscera, and aids thus in blood and lymph circulation. Dally[2]

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(1) Journal Anatomy and Physiology, April, 1905.
(2) Lancet, June 27, 1903.

and Hasse[1] have shown that the heart and the root of the lungs move downward and forward with inspiration, drawn by the diaphragmatic movements. Laterally and posteriorly the sternal and dorsal bands of fibers are prone to leave an opening which may allow the escape of the contents of one cavity into the other. It is more frequently closed by a membranous diaphragm.

Much evidence in support of this view is found in the collection of material to be found in Ballantyne's treatise.[2] The long expansion of the neck and chest, and the body development required by the upright posture of man and the anthropoid apes, materially changes the muscular development of the trunk, and also changes the structure of the diaphragm. Much is learned from study of the lungs in the tailed amphibians. The lungs in birds have an anterior or pulmonary and a posterior or sacculated portion. There is the same differentiation in the case of the tortoise, but it is less sharply outlined. The sacculated portion is situated within the abdomen, the pulmonary portion is within the thorax. Air is drawn into the pulmonary portion, and at the same time the foul air is drawn into the sacculated portion, from whence it is expelled. The sacculated part does not participate in the interchange of gases.

In the human subject this sacculated portion has disappeared, but there are three indications of its former existence: (1) If the blood vessels of the bronchio-arterial source be injected satisfactorily, in the region of the mediastinum and of the diaphragm, there will be noted a rich arterial anastomosis in the subpleural tissues. It is not to be seen elsewhere. (2) The diaphragmatic openings and weak places are points of potential hernia. (3) The infundibula are the *anlagen* of the saccular portion. It is probable that these alone expand and contract with respiratory movement; the sacs are emptied and filled by diffusion.

Early in ancestral development the lungs lie posterior and inferior to the heart. The origin and insertion of the ligaments and vessels in the human subject give emphasis to this point. The lungs have come out of the abdomen and into the thorax by a partial perforation of the cervical wall or diaphragm at the two pleuro-peritoneal openings. This diaphragm is the cervical part of the abdominal aponeurosis. The anterior part of the septum transversum is the same as in amphibians. The posterior part is composed of fusion of a part of the amphibian cervical with the dorsal wall of the pericardium. A part of this aponeurosis is perforated, but is pushed upward before the lung.

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(1) Die Formen des Men. Körpers, etc., Jena., 1888-90.
(2) Manual of Antenatal Pathology, ii, p. 477.

In certain higher forms the apices of the lungs come to lie well above, and posterior to, the heart. This portion of the lungs is relatively poorly supplied with mechanism for respiration and for exchange of blood. As we rise in the scale of life we reach a point where the apices have developed, but there is no rib development to provide for movement. At this stage the downward pull of the diaphragm transmitted through the pericardium and the mediastinum is the means of emptying the apex of the lung.

Nothing could be more interesting than this study of the varying structure and functions of different parts of the respiratory apparatus. The central idea of respiration is an interchange of gases between the blood and the tissues. And this is the factor which has obtained in the evolution of the respiratory apparatus. The diaphragm, to begin with, was a blood-moving structure. It is largely so at the present time. The study of Schroeder and Green[1] is confirmatory of this opinion.

The ribs themselves were developed in order to assist in the shifting of the blood mass. In certain animals their function is to enlarge the body cavity; in others they compress it. They develop in the middle muscular sheet of the body, and are by no means limited to the thoracic region in lower animals. They began to develop at a time when tailed amphibians had a trunk musculature arranged so that some means of expansion of the body became a necessity. Therefore the early function of the ribs was expiratory. At different stages of evolution filling the lungs with air and filling them with blood have varied in

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(1) American Journal of Medical Sciences, Feb., 1902.

their relations to each other—at times the thorax movement has filled the lungs with air, has emptied them of blood, and at others they have been emptied and filled with both air and blood by the same movement.

A study of the origin and distribution of the phrenic nerves in man, in connection with a study of the nerves and muscles of the lower animals, convinces Keith of the correctness of his idea as to the derivation of the diaphragm. He is not entirely certain as to why the phrenics fuse, but that they have fused is shown by the distribution of their branches, and the frequent separation into two portions before the diaphragm is reached. (The septum transversum he regards as an assistant to the heart.) He says the heart of the fish is merely a respiratory pump. In these lower animals a broad, firm membrane which can be dragged back and forth is capable of much help to the circulation of blood.

The author believes the structure commonly called the pleuro-peritoneal membrane, and also the dorsal diaphragm, is merely a crescentic fold of peritoneum forming part of the genital mesentery, and running to the old Wolffian body—at one time it rendered support that was needed. The presence of this structure confirms Keith's opinion that the liver, diaphragm and umbilicus are the central points away from which the lungs, head, genitals, etc., have migrated.

Lumbar Arteries. The lumbar arteries are obviously somatic segmental branches of the abdominal aorta, according to Young.[1] They correspond to the intercostal branches of the thoracic aorta. From a study of a number of cases, Young disagrees with Thane's statement (frequently repeated in text-books), namely, that the middle sacral is a continuation of the abdominal aorta and often gives off one or more lumbar arteries. Young shows that the sacral is in reality given off by the lumbars rather than vice versa. Occasionally one sees a sacral artery bearing such a relation to the aorta and the lumbar artery as to make it difficult to say which one gives off the other.

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(1) Journal Anatomy and Physiology, April, 1905.

The matter is more important from its embryologic bearings than from any clinical considerations.

Abnormalities in the Form of the Kidney and Ureter. Pohlman[1] bases a classification of congenital kidney anomalies upon embryologic considerations. His article should be read in its entirety. He considers only the anomalies that originate before the third month of fetal life. The steps in the earlier development of the kidney are as follows:[2]

1. The renal bud arises dorsally on the Wolffian duct, after the duct has reached the cloaca, and at a short distance from its entrance.
2. The buds grow dorsally and they lie closely together, each being capped by a specialized mesodermic tissue, the renal mesenchyme.
3. Each bud divides into an upper and lower sprout at some distance from the Wolffian duct.
4. The kidney wanders upward from a position in front of the second sacral vertebra, rotates at the mid-lumbar region, and finally reaches its normal height at about the end of the second month.
5. The kidney becomes vascularized after it reaches its normal height.
6. The ureter changes its position on the Wolffian duct from dorsal to lateral, and finally comes to empty distinct from it.
7. The ureter loses its relation to the Wolffiar duct entirely and comes to empty higher and more laterally.

These complex developmental stages are responsible for frequent departure from the average arrangement of the kidney and ureter. Usually these are discovered post-mortem, occasionally they are of clinical interest. Pohlman, as the result of these anatomic and embryologic studies, evolves the following rules:

When there is incomplete double ureter the rule is as follows: The pelves of the kidney are always distinct, the ventral ureter arises from the upper pelvis and there is one orifice which is usually normally placed. The rule for complete double ureter is: The relation of the two ure-

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(1) Johns Hopkins Hospital Bulletin, February, 1905.
(2) American Medicine, June 18, 1904.

ters and pelves are the same as in incomplete reduplication, and the ureter from the upper pelvis has the lower orifice in the bladder and lies somewhere between the opening of the dorsal ureter and the genital duct.

The form of the kidney is not affected by abnormalities of the pelvis. On the other hand, in all marked congenital variations in the form of one kidney the ureter is either completely or incompletely doubled.

The kidney is always prone to take shape from its surroundings. In addition, there are anomalies which are due to irregularities in the development of the renal bud. Should the stalk thereof divide too early, there is liable to be two mesenchyma masses situated one above the other, and these are prone to remain as two separate organs or to fuse incompletely or completely, before rotation, in the midst of rotation, or after rotation.

The renal buds, right and left, early in embryonic life are quite close together. These mesenchyma masses are quite prone to fuse in whole or in part. Sometimes it happens that one or both buds will divide irregularly (as noted previously), and then fusion more or less complete will occur.

SECTION II.

PHYSIOLOGY.

Gastrointestinal Canal. Mendel[1] *discusses the newer physiology of the intestinal canal.* The interdependence and coöperation of different physiologic tissues has not been given just consideration by the modern physician. A consideration of alimentation is more than a mere study of the solvent action which the digestive secretions exert.

Innervation and Movements. The older view of stomach motility, based on the experiments of Beaumont on St. Martin, that the food passes along the greater curve, starting at the cardia, and then along the lesser curve, has been much changed by x-ray observations on the living organ. These show a difference of action at the cardiac and pyloric ends. The cardia grasps the food and holds it in a tonic grasp, while at the pylorus there is active peristalsis. At intervals the sphincter opens and portions of the contents escape. This observation gives acceptance to views that salivary digestion is continued in the stomach for some time. Acidity is marked at the pyloric end, but is absent at the cardiac.

Bayliss, Starling and Connor have presented new observations on the movements of the intestines. These are shown not to be continuous, but to occur in an irregular manner, so that constrictions separate the bolus into masses for variable periods; these may unite or be again pushed onwards, as an independent collection of contents. The inhibiting action upon muscular activity by the reaction of the intestinal contents is interesting. Acid in the stomach causes the pylorus to relax, while in the intestine the degree of reaction modifies the movements.

The Glands. The study of gland secretion has recently added much to our understanding of digestion. The matter of gland secretion is almost entirely reflex. The intro-

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(1) Jour. Amer. Med. Ass'n, Nov. 19, 1904.

duction of indigestible or chemically inert substances into the intestine gives rise to secretions of unusual amounts and often lacking in physiologic constituents. The application of particular kinds of foods always calls forth the particular ferments required. The character of the food applied in an experimental animal will completely change the character of the secretions formed by its presence. There is a marvelous interaction, and it seems true that the presence of the finished digestive substance acts as a strong inhibitor of secretion to the same extent as raw food excites it. We see in this much more than the simple mechanical force that has been the chief factor heretofore considered, but that there is a most complicated chemico-nervous activity involved.

Chemistry. In the stomach the study of the continuance of ptyalin activity has brought out the presence of a lipolytic ferment in this organ and the digestion of fats. Proteolysis has been shown to have a possible cleavage much beyond what was formerly considered the end. The chemistry involved in the absorption of peptones and other products of proteolysis is, also, one deserving more study. There is a marked difference in the degree of absorption that takes place with or without the presence of digestive enzymes. This point has great bearing on artificial feeding. Elimination into the intestine has received much deserved consideration. Good has shown that lithium is excreted more rapidly into the stomach than by the kidneys. MacCallum's observations regarding saline purgatives show that the intestines excrete different salts in different areas. Moreover, the contents in the lower bowel must be considered as more excretory than mere food residue.

Mendel[1] further discusses this subject in another paper. From whatever standpoint the chemical processes are reviewed the enzymes or the soluble ferments demand the most important place among the active agents involved. Their exact chemical nature is still doubtful. There is a growing tendency to regard enzymes as a special type of

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(1) Medical News, May, 1905.

catalytic agents, colloidal in nature, which are subject to the general laws applicable to the inorganic catalyzers. There exists a marked correspondence between catalysis and enzyme action in respect to laws of velocity of reaction, optimum temperature and dependence upon external influences. An enzyme solution which is able to bring about a partial hydrolysis of fat can rebuild these fats from their cleavage products. Similar reversions have been obtained with sugar-splitting enzymes. If proteolytic enzymes have a reversible action and are able to resynthesise proteids from the products of proteolysis an important addition to our knowledge of anabolism has been made. It is a current impression that fats are not attacked in the stomach and that the gastric juice has no lipolitic properties. Ludwig thought the cleavage of fats in this organ was the result of bacterial origin. Others have found fatty acids and soaps in the stomach after the ingestion of milk and they attribute to the stomach the power to liberate fatty acids with the loss of its fat splitting enzyme. The enzyme is very sensitive to pepsin, HCl, heat, and its action seems to be influenced largely by the perfections of the emulsion of fat. Moreover, there is some evidence of the existence of a zymogen of the stomach—lipase.

Cohnheim discovered a soluble ferment furnished by the small intestine capable of further splitting the primary cleavage products of proteids, albumose and peptones into their crystallin nitrogenous derivatives, and called it "erepsin." It does not act on native proteids, is abundant in the mucosa and scant in the secretion; its action is exerted upon the products of proteolysis in their slow passage through the epithelial cells during absorption.

Two newer features of chemical physiology of enzymes, deserving of mention, are the specificity of the soluble ferments and the existence of anti-enzymes. Animal parasites elaborate specific substances, which can inhibit the action of pepsin and trypsin. Anti-enzymes resemble anti-bodies in various respects. Extracts of the stomach and intestines like extracts of intestinal parasites, check the proteolytic power of pepsin and trypsin in artificial digestive experiments. A new factor in the protection of the body against its own secretions and its bearings upon the pathology of the alimentary canal can be surmised.

The most important contribution to the physiology of digestion lies in the mechanism and chemical regulation of the secretion and organs engaged in nutrition. The activity of the salivary glands is excited reflexly, according to the nature of the food present in the mouth. Mucous membranes are not indifferent to the composition of the ingested substances, and they seem to act as if endowed with discriminating sensibilities for the different food stuffs. What are the excitants of pancreatic secretion? Bayliss and Starling have shown that the pancreatic secretion is called into play—not through extrinsic nerve channels—but by a chemical substance formed in the mucosa of the upper part of the small intestine, under the influence of acid, and is caused by the blood streaming to the gland cells of the pancreas; this is called "secretin." Although not completely isolated and identified, it is obtained by extracting the mucosa with 0.4 per cent HCl. A small amount injected into the circulation suffices to call forth a copious flow of pancreatic juice. This is not due to the HCl, for this alone provokes no secretion. Secretin can be boiled and neutralized without changing its activity. It also stimulates the flow of bile. We are now easily enabled to form some synthetic conception of the events which succeed each other in the digestive cycle.

The stomach contents combined with HCl and the food masses poured out into the duodenum through the relaxed pylorus induce a flow of pancreatic juice, bile and—according to some authors—enteric juice.

An excessive discharge of acid chyme is prevented by the reflex pyloric mechanism which keeps the pylorus closed; meanwhile the chyme is neutralized and the chyme escapes. Pancreatic juice contains little, if any, proteolytic enzymes. In its place zymogen and trypsinogen are present. Trypsinogen is activated by a peculiar enzyme, called enterokmase, belonging to the class of enzymes called kmases or zymolysins, capable of activating zymogens. In addition to chemical regulations of the secreting processes there are functional adaptation on the part of digestive glands to the work which they are called upon to accomplish. Food being variable daily, in regard to order, odor, flavor and composition, these changes in digestion adapt themselves daily.

Perhaps the most striking feature of the present development of the study of digestion is the increasing complexity with which the explanation of the function is attended. Yet the unraveling of the details of these interesting chemical and physiologic reactions gives promise of a clearer understanding of the ensemble of processes termed digestion.

Mechanism of Digestion. Camo[1] discusses recent advances in the knowledge of the *movements and innervation of the alimentary canal.*

The mechanical factors in digestion perform three chief functions. The movement of the food through the alimentary canal; the mixture of food with digestive juices and bringing it in contact with the absorbing mucous membrane. Peristalsis is the general action by which these functions are effected. Where digestive juices are lacking and absorption does not occur, as in the esophagus, the food is moved rapidly. On the other hand where digestion and absorption can take place, rapid progress is prevented by the sphincters of the recurring peristaltic waves passing over towards the closed sphincters and serve to mix the food with the digestive juices, as in the stomach, or expose the food to the absorbing mucosa, as in the ascending colon. In the lower intestine, with no sphincter present, peristaltic activity is infrequent, and mixing takes place by the rhythmic contraction of circular fibres.

Movements of the Alimentary Canal. The Esophagus. As the name implies the esophagus merely serves to transmit food from one digestive organ to the other. It was supposed that a morsel of food was thrown down the esophagus by the action of the mylohyoid muscle, and that the esophagus was merely supplementary to force the particles along. But Kronecker and Meltzer have shown that the transmission of food particles towards the stom-

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(1) Med. News, May 20, 1905.

ach was accomplished by contraction of the esophagus. According to them it is divided into three parts: a cervical, middle and lower part. These contract in succession; after digestion begins, the rate being different in different parts. Schneiber finds no separation in three parts, but his curves reveal a constriction. This moving constriction can only be explained as a peristaltic wave, the wave in the neck lasting 3.5 seconds, in the thoracic region 5.9 seconds. He contends that the wave moves more rapidly in the cervical portion than in the thoracic portion. This is confirmed by Moser and the author.

The Cardia. The cardiac sphincter is stated normally to be in a state of tonic contraction. The author has seen rhythmic relaxation of the cardia in cats so that fluid food streams from the stomach into the esophagus above the level of the breast, then is pressed into the stomach again by the peristaltic wave, only to be released a moment later to pour again into the esophagus. This occurred at intervals of one to two minutes. The function of the cardia, therefore, may be to keep the passage into the stomach free from an accumulation of the swallowed food so long as the sphincter remains contracted to prevent regurgitation of gastric contents.

The stomach is a region of storage for food and also one in which the proteid and carbohydrate digestion may occur. It consists of two parts: the cardiac and pyloric. The pyloric part is characterized by continued peristaltic waves passing over it during digestion, while the cardiac part is without them, but as the food passes over the muscles of the fundus this by tonic contraction squeezes the contents into a more motile division. The rate of peristaltic waves varies. The efficiency of peristalsis in mixing food with gastric secretions depends upon the contraction of the pyloric sphincter, so long as it holds each constriction-ring coursing from the middle to the end of the stomach and presses the food into a fluid pouch. The food, unable to escape through the pyloric ring, has as its only outlet the opening in the advancing ring. This is an admirable device for burying the food under the glandular secretions of the pyloric region, for, as a constriction occurs, the secreting surface enclosed by the narrower muscular ring is pressed close around the food within the ring. As the constriction advances it presses inward fresh glandular tissue, making a food stream sweeping in one direction pass an ever refreshed mucous surface moving in the opposite direction. Thus the food at the pylorus is thoroughly mixed with gastric juice.

The cardiac end is the reservoir for food. The food remains unmixed with gastric juice, and so remains for at least two hours.

The Pylorus. Observations have shown that there is an intermittent closure of the pylorus. The channel is usually closed, although it occasionally opens, and when open peristaltic waves propel the food into the intestine. It has been proved that fats remain long in the stomach and that discharge begins slowly. Carbohydrates leave the stomach soon after their ingestion, while proteids take from one to two hours to leave the stomach, and not even then. What agency causes the pylorus to relax? Free acids in the stomach open the pylorus and initiate the chemical control of the sphincter. This permits the exit of the acid chyme. The acid is neutralized in the duodenum and the pylorus relaxes. Thus carbohydrates go early and quickly into the intestines to meet their proper ferment. Proteids postponing the presence of HCl by uniting with it, would be retained in the stomach to suffer gastric juice alteration, and only after such alteration, be permitted to go on. Thus the intestine would be saved from overwhelming discharge from the gastric reservoir.

The small intestine is a region of digestion and absorption. There are no sphincters. Peristalsis cannot act to mix the food. The author calls the process "rhythmic segmentation." There is left, then, peristalsis. The movements of the intestine are described as rhythmic narrowings and shortenings of the gut, alternating to-and-fro movements of the long axis without changes in the lumen; local or extensive periodic contractions and relaxations mainly of the circular musculature, and waves involving both muscular coats, traveling downward rapidly. This mixes the food and exposes it to the mucosa.

Stomach Functions. The test for *functional activity* of the stomach, as proposed by Sahli,[1] and called the *"Desmoid Reaction,"* consists in enclosing methylene blue or iodin in a bag of goldbeaters' skin. If the stomach activity is normal the bag will be digested, and the reaction of the contents may be noted in the urine in a few hours. This method has been recently modified by using dentist's dam, tied with fine catgut and containing:

Methylene blue	.05 gram
Iodoform	.1 gram
Pulv. licorice	.04 gram

This makes a small pill to be swallowed. The catgut is digested and the contents liberated. A positive reaction in health can be obtained the same evening if the pill is taken at noon, and can be shown both in the urine and saliva.

Passage of Foodstuffs from Stomach. An article by Cannon[2] describes experiments showing manner in which foodstuffs are moved from the stomach into the small intestine. His method consisted in feeding young, healthy cats that had been starved, with a definite amount of food, either proteid, fat or carbohydrate, mixed with bismuth subnitrate. Exposures by x-ray were made at intervals of one-half to one hour, and the shadow areas studied with the fluorescent screen. The food was made into a pasty mass of about the same consistence in each and measured 25 c.c. with 5 grams bismuth subnitrate added. The cats were stretched out and the fluoroscope pressed against the abdominal wall, so that the intestines should be as near parallel as possible and as fairly free from folds. Between 600 and 700 readings were made. An illustrative table shows the length of shadow of the intestinal contents at the times indicated after eating:

Hours after feeding—	0	½	1	2	3	4	5	6	7	
Fats	.0	5	9	14	17	16	13	13	9	cm.
Proteids	.0	1	5	18	21	23	19	17	14	cm.
Carbohydrates	.0	8	30	39	33	25	19	14	6	cm.

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(1) Correspondenz-Blatt Schweizer Aerzte, XXXV, Nos. 8-9.
(2) Jour. Amer. Med. Assn., Jan. 7, 1905.

The carbohydrates and fats left the stomach early, the former rapidly and the fats more slowly. The proteids were retained, frequently no discharge at all in the first half hour. Other tables corroborated this result. At the same time the peristaltic waves in the stomach wall continued regularly, although nothing passed from the pylorus. Food that is not acted upon to any extent passes quickly through the stomach, while that digested here is retained. The peristaltic waves churn the food and if the pylorus is opened force it onward. Their variation is dependent only upon the amount and not upon the kind of food. The excretion of HCl and the presence of food in the stomach cause the pylorus to open and discharge the contents, and in the duodenum causes closure of the pylorus, so the action of the sphincter is automatic. It is, indeed, a matter of chemical stimulation. The action of fats and carbohydrates is explained by the fact that the former, in the duodenum, has a mild closing stimulation as regards the pylorus, and in the absence of opening stimulation they tend to be retained. Carbohydrates cause acid secretion, but do not unite with it, and, therefore, give rise to a more active opening stimulation, while, at the same time, starches induce the pancreatic secretion to be discharged, which neutralizes the acid quickly.

Lymph Flow from Pancreas. Bainbridge[1] used the extract of the duodenal mucosa, called "secretin" by Bayliss and Starling, with a view to studying lymph flow from the pancreas. By the use of this extract it is possible to obtain pancreatic juice at will. His method consisted in anesthetizing dogs with the A. C. E. mixture, opening the abdomen and placing cannulas in the main pancreatic duct and in the thoracic duct, then closing the abdomen. A cannula for the injection of the extract was tied into the jugular vein and a manometer attached to the femoral artery. The animals had been previously starved, causing the pancreas to be at rest and the lymph free from fat. The injections of extract were made slowly from a burette, about 1 to 2 c.c. per minute. The experiment generally lasted about 20 minutes.

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(1) Brit. Med. Jour., Dec. 31, 1904.

If secretin be injected rapidly it causes muscular contractions, dyspnea and rapid fall in blood pressure. When injected slowly there is no such result. The increased flow of lymph begins about 10 to 20 minutes after the starting of the extract injection, reaches its height in 20 minutes, and lasts altogether about one hour. The flow is two or three times what it was before the injection. Ileum extract also increases lymph flow, but it is less active than secretin. In the first experiments the flow of lymph recorded before injections was from 1.5 to 3 c.c. for 10-minute periods, and after injection of secretin it was from 5 to 9 c.c. for similar periods. After ileum extract the flow was from 2.8 to 5 c.c. for the 10-minute periods.

After ligature of the portal lymphatics secretin solutions still caused an increased flow of lymph, while ileum extract had practically no effect. As both of the extracts contain depressor substances, as bile salts, it is very certain that the effect in this experiment was due to the specific body secretin itself, and not to the depressing influences of other constituents of the extracts. Further, the lymph formed in this case must have been formed either by the intestine or the pancreas.

When the thoracic and pancreatic lymphs were collected simultaneously, it was found that the variation in flow was very similar. However, the secretion of pancreatic juice reaches its maximum and falls earlier than the thoracic lymph flow.

As regards the manner of action, the writer considers that the action of secretin is specific for the pancreas, and that it has practically no action on the intestine. The close relation between the flow of lymph and pancreatic secretion would support his view. The vaso-dilator action of the extract on the pancreas may cause the lymph flow, or it may be due to metabolic changes during the active formation of secretion, causing an over filling of the lymph spaces. The writer considers the latter view as being the more plausible.

Protective Value of Proteids on Trypsin. Vernon[1] found that in an alkaline solution of trypsin, about 56 per

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(1) Brit. Med. Jour., Sept. 14, 1904.

cent of trypsin is destroyed in one hour when kept at 100.4° F. When various proteids are added a preservative influence is noted. By determining the amount of ferment remaining at the end of the hour this influence can be measured. Native proteids have relatively the least effect; hydrated proteids are more protective, while decomposition products have the highest influence. Increase in the amount of proteid in the mixture proportionately preserves trypsin. It was found that this property depends upon the power of the given substances to neutralize alkalies. If the acid radicles are previously neutralized all protective power is lost. Aspartic acid has a somewhat higher value than proteids, but bile acids have less value.

Liver Cells. Changes During Activity. Carlier[1] experimented with a view of learning more as to the formation of ferments by the liver cells. His method consisted in feeding 50 white rats for some time on a mixed diet; they were then divided into four groups. The animals were caged individually. One group was continued as before, another was fed on lean meat, another on starch and sugar, and the last on suet. After continuing these special diets for some time, 1 animal in each group was starved somewhat, and killed as a control. The others were then killed, hour by hour, until all were used. Sections of the liver were made and studied by various stains. The liver cells in fasting animals were found with distinct cell walls and completely filled with protoplasm, there being practically no vacuolation. Situated in the protoplasm were lumps of a structureless substance, the nature of which the author could not determine. This substance was stained deeply with eosin and iron-alum hematoxylin. It did not give glycogen reactions. It was found most abundant after a long fast. There were also seen in many cells minute, highly refractile granules, of a greenish gray color, situated between the nucleus and the bile capillaries. The nucleus is oval, plump and poor in chromatin. It contains several nucleoli and some of these may be seen migrating through the nuclear wall. Some cells contain several nuclei. During activity, one of the first things

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(1) Brit. Med. Jour., Sept. 24, 1904.

observed was a disappearance of the highly refractile granules, and they do not reappear, even after 12 hours. It would seem that they accumulated during fasting. The most visible change in the cytoplasm was in the formation of vacuoles. These appear within an hour after feeding, and do not disappear for one or two hours after the beginning of fasting.

In the starch-fed group of animals particularly, the cells became swollen at about the sixth hour, and the vacuoles showed an abundance of glycogen. A marked change in the nuclei takes place, exhibiting all the changes of chromatin loss and repair. The direction of their activity is evidently in the production of some digestive ferment, but not in the form of granules, as occurs in the stomach. Chromatin activity was found to be in two stages, the first directly after feeding, the other beginning 4 or 5 hours later. Between these periods the nuclei are completely restored. The second stage of ferment activity was longer and more marked, evidently more ferment was produced. In all of the animals, that is, in each group, the same changes were observed, but there was a variation in intensity; it was less evident on a starch diet than on proteid and fat rations. The first stage may be considered as psychic in origin, being similar to that seen in the stomach and salivary glands, when stimulated by the sight of food.

Digestive Activities. Allchin,[1] in discussing *food,* considers that, for the maintenance in structural integrity and functional activity of the bioplasm, the food supplies must be of a more complex character than is absorbed by plants. Proteids, carbohydrates, fats and some salts are equally necessary to animal and vegetable protoplasm, which, therefore, correspond closely in essentials. In plants there is greater extent of preparation of the ingesta before they are finally made use of. The range of synthetic capacity of the plant is so far greater; animals start with their food where plants leave off, the ultimate form of material presented to the bioplasm being similar in both cases. The nutritive requirements of the animal organism are such

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(1) Lancet, April 5, 1903.

that the food should contain certain proportions of different substances which correspond to the materials of which we have seen that living matter is composed. A satisfactory diet should, therefore, consist of proteids, carbohydrates, fats, salts, water, oxygen. Although fats and carbohydrates may in a general measure be made to replace each other or may be entirely withdrawn from the dietary, such modifications can only be tolerated for a limited period and are prejudicial sooner or later to the animal.

Each foodstuff is necessary, though, perhaps, in a modified degree. The proteid is of prime necessity. This fact of proteid requirement implies that the animal organism is unable to synthesize from simple nitrogenous substances —such as ammonia or the nitrates obtained from the outside and ingested as such—the complex proteid molecule which is the chief component of its protoplasm. Plants, especially those containing chlorophyl, are enabled to construct their proteid constituents from such simple nitrogenous compounds as the nitrates, particularly the ammonium salts. Certain bacteria assimilate free nitrogen freely. In this case the range of synthetic power is at its maximum. The organism feeding on the chemical element itself and ultimately building up the complex proteid. On the other hand there are some parasitic and saprophytic fungi absolutely dependent upon some form of proteids, peptone or others, supplied as such, approximating in this respect to the animal requirements. Although the carnivora exist upon an almost pure proteid diet, this could not be applicable to man, for in such a case, in order to obtain the requisite amount of carbon and hydrogen, such an enormous amount of meat or other proteid food would have to be eaten as to be almost prohibitive, owing, partly, to the difficulty of its digestion, and partly to the ill effects such a food would entail in various directions. Hence a pure meat diet falls short in the requirements as regards C. and H., which, consequently, are supplied by the adipose of the individual, which is rich in these elements. Therefore, the carbohydrates and fat are of absolute necessity and help balance the nitrogenous equilibrium, and are known as "proteid sparers." In considering the food, therefore, account has to be taken not only of that which is taken into the body, from time to time, but that which is already stored up for a time before being presented to the living matter for disposition.

Of the inorganic salts sodium chlorid is the only one added during the preparation of the food or its digestion. The phosphates are derived from some organic compound of the bioplasm. The other salts arising from the material ingested or from the bioplasm direct.

Regarding the quality of aliments necessary to maintain a state of metabolic equilibrium and a condition of well being it is found that more food is taken than is generally required. In one of the latest works in dietetics (by Hutchinson), it is laid down that the requisite diet for a man of ordinary weight doing a moderate amount of muscular work should be of value in potential energy of from 3,000 to 5,000 calories, and that for such an individual the daily consumption of proteids should never be allowed to sink below 100 grams, but should preferably be 125. The amount, of course, must be guided by the degree of thorough mastication, as, also, its qualities.

Relation of the Bioplasm to the Ingesta. Foremost among the fundamental notions is that the living matter in mass—as also in its constituent molecules—consists of a permanent part which is not concerned in the performance of function, and of a collateral part which is used. The permanent part undergoes a certain amount of wear and tear, which necessitates its repair, while the collateral part is of a higher degree of chemical complexity than the ingesta which are destined to replace it and maintain the supply of fuel material which has undergone disintegration. While the precise condition of the living molecule is quite unknown to us—it is into the synthetic (anabolic) and analytic (katabolic) changes that light is gradually penetrating. In the carrying out of the synthetic changes kinetic energy is required, that is, the energy which becomes potential in the advancing molecule, later to be again converted into kinetic, as the molecule undergoes decomposition. The requisite energy being derived from the heat and chemical energy liberated in the course of katabolism. The following illustration will suffice: Indol is a product of proteid decomposition, which is readily formed by certain bacteria in the intestines. This same result can be obtained by fusing proteids with caustic alkalies.

It is the dependence of the synthetic processes upon the energy supplied by katabolism that both anabolism and katabolism are, in a great degree, coincident, and in a measure mutually involved. So far as we know, it is by chemical energy that synthesis is effected in the animal body, just as muscular work is accomplished by the transformation of a corresponding amount of chemical energy. But while a complex series of anabolic changes intervene between the nutriment, as taken into the body and its final incorporation into the protoplasmic molecule, changes closely related to those of a katabolic nature, resulting in the reduction of the body, waste takes place, there still remains the incorporation in the molecule of the pabulum. The plausible hypothesis is that of assimilation with which the name of Ehrlich is associated. He conceived that in the protoplasmic molecule were certain atom groups, which abstracted, presumably chemically, corresponding atom groups of the protoplasm are excited to formation, as the response to the presence of the nutritive material. To another atom group he conceives the ferment is attached, constituting, as he terms it, the "complement," by the action of which the actual assimilation is accomplished. An extension of this hypothesis constitutes his side chain theory of immunity.

Changes in the Ingesta. The author's next step is to consider the successive changes undergone by the ingesta, from their intake to their assumption by the bioplasm, as far as is known. The first of these is known under the term "digestion." It is the function which is concerned with the conversion of the ingesta into such a fluid and diffusible condition as to fit them for absorption into the blood current, which is an essential preliminary to their assimilation by living cells. Except the inorganic foodstuffs, the proteids, fats, and carbohydrates require more or less digestion. It is not probable that the absorption of the foodstuffs depends upon osmotic pressure alone, but that the living tissue elements exercise some vital share in effecting the absorption.

The digestive changes in the alimentary canal are brought about by special glands pouring out their secretions in the mouth, stomach and intestines, their efficacy depending upon special ferments or enzymes which they possess, and which are products of the metabolic activity of the gland cells. To a similar source the HCl of the gastric juice is attributed, the chlorid of the food being forced upon the parietal cell of the peptic glands, probably by the action of the alkaline phosphates. The change of the several ferments determined in the various alimentary principles is in the nature of hydrolysis. For their satisfactory action a temperature corresponding with that of the body is necessary, as is also a fairly constant state of acidity and alkalinity of the medium, according to the special secretions. Thus, pepsin and rennet formed by the central cells of the gastric glands, act best in the presence of 0.2—0.4 per cent HCl, while the pancreatic enzymes—trypsin, amylopsin and steapsin—are destroyed in the presence of an acid. The ptyalin of the saliva requires a neutral or slightly alkaline reaction. To show the still further complexity of conditions obtaining in the gastrointestinal tract, it has been found that several digestive ferments are, to some extent, protected from the destructive action of acids, alkalies and high temperature, by the presence of proteids. This is the result of the proteid combining with the acid or alkali and so preventing its reaction in the ferment—so the efficiency of the ferments is insured against any injurious conditions which might occur. Through Pawlow we have been led to realize the progressively interdependent character of the successive stages of the process of digestion. The special stimulus to the pancreatic secretions is the gastric juice, and Starling has shown a new substance, called by him "secretin," which is formed in the duodenal cells and which exerts a stimulating action on the pancreatic secretion.

Briefly stated, it seems that the quantity and quality of any juice are determined by the aliment, and that different foods excite the secretion of food differently. Thus, the secretion following a meat diet differs from that following a bread diet—showing that the gastric juice comes to be modified, according to the food taken.

Among the recent extensions of our physiologic knowledge, that concerned with the digestive ferments is of the greatest and most important interest, as it helps to study the real change the food undergoes. The relation of the enzymes to one another, the responses of the living cells to the various demands made for ferments of different power, while at present only imperfectly recognized, yet sufficiently suggest greater possibilities in our truer conception of the intricate nature of the living processes, and to exhibit more clearly that reaction between living matter and its environment as the fundamental condition of vital activity. That capacity of the bioplasm to form an antitoxin, when exposed to a toxin (which, in such a case, expresses protective action), is wholly comparable to the formation by that same bioplasm of an enzyme or zymogen which shall deal with the nutrient matter submitted to it for its own advantage and maintenance. And as one injurious agent determines the formation of something which shall render it inert, so may the requisite food call forth the reagent most suitable to effect such changes in it as shall render it useful to the living molecule.

Intestinal Antisepsis. The effect on the *excretion of hippuric acid* in the urine has been studied by Pragen.

In 1824 Wohler furnished the first true example of a synthetic process occurring within the animal organism. He showed that when benzoic acid was introduced into the stomach it appeared as hippuric acid in the urine. This synthesis may be expressed as follows: Benzoic acid plus glycocoll equals hippuric acid plus water.

Gomerman has shown that gelatin on decomposition yields 9 per cent glycocoll. Fischer found 16 and Levene 20 per cent. In addition it yields amido acids, such as leucin, aspartic and glutanic acid, also phenylacetic and phenylproponic acid, but no indol or skatol, in which respect it differs from proteids. The purpose of the experiments was to determine:

1. What effect the feeding of gelatin had on the excretion of hippuric acid in the urine.
2. The effect on the excretion of hippuric acid when there was putrefaction going on in the intestinal canal.
3. The effect on the excretion of hippuric acid when the intestinal canal was made antiseptic by the use of calomel.
4. The effect of intestinal antisepsis on excretion of nitrogen.
5. What effect gelatin had on burning of tissue in the body.

Hippuric acid was so called by Liebig, because he first found it in the urine of horses. It occurs in large amounts in herbivora and small amounts in carnivora. This may be partly explained by the fact that vegetable food contains large amounts of aromatic substances, which, upon oxidation and reduction, yield benzoic acid. This benzoic acid unites with glycocoll and forms hippuric acid.

Although the question of where the hippuric acid is formed has received considerable attention, no positive proof has been advanced as to the exclusive place for this synthesis. It has been said that it occurred not only in the kidney, but also in the intestines. It is found in all intestinal diseases and in intestinal putrefaction. The experiments consisted in feeding dogs with gelatin, after they had been starved several days, and by using calomel as an intestinal antiseptic, observing the increase in hippuric acid. The results:

1. The feeding of gelatin alone increases the excretion of hippuric acid.
2. When putrefactive changes are increased the excretion of hippuric acid is also increased, and vice versa.
3. When the intestinal canal was made antiseptic with calomel there was practically no hippuric acid excreted.
4. Intestinal antisepsis has no effect whatever on the excretion of nitrogen.
5. No matter how much gelatin was fed it was completely burned and some of the body's proteids with it.

6. Therefore, gelatin never builds up any tissue, although it may to a certain extent protect the body's proteid from decomposition.

Force of Contraction of the Gall-Bladder. Freese[1] found that the gall-bladder of the dog is capable of equaling the resistance of a column of Ringer's solution at 1,004 sp. gr. 8½-12½ in. high. It had been shown by Heidenhain that the secretion pressure of the liver was 7 1-3 to 8½ in. of water. It will be noted that the bladder has practically no muscle power in the dog in excess of the secretion pressure of the liver. As a further comparison Mosso has shown that the urinary bladder is strong enough to support a column of water 78 in. high. As a further study Freese demonstrated that the muscle wall has constrictor and inhibitory fibres, which travel through the splanchnic nerves. They arise from the cord in the 6th to 13th dorsal roots. The constrictor fibres come out mostly in the 10th, 11th and 12th roots. The dilators mostly from 8th to the 12th.

Chest Measurements and Lung Capacity. There is constant interest in chest measurements and the practical results to be learned from them. Malone[2] presents an extended number of measurements and considers them as relations of chest contour to lung capacity. The chest pantograph[3] was used for taking the measurements. The observations recorded were:

Thoracic diameters:

Dorso-ventral, inspiratory and expiratory.

Transverse, inspiratory and expiratory.

Contour areas, chest pantograms.

Contour index, determined by the formula of Hutchinson (dorso-ventral diameter divided by the transverse diameter).

Lung capacity.

Tabulation and arrangement of the data results in the following comparisons for the two principal anatomically distinct chests—broad and deep:

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(1) Johns Hopkins Hospital Bulletin, June, 1905.
(2) Jour. Amer. Med. Ass'n, Sept. 17, 1904.
(3) Practical Medicine Series, Aug., 1904.

THE RELATION OF CHEST CONTOUR TO LUNG CAPACITY.

Observations.	Class 1. Small Chests.		Class 2. Medium Chests.		Class 3. Large Chests.	
	Broad.	Deep.	Broad.	Deep.	Broad.	Deep.
Contour index $=\frac{\text{D. V. Insp.}}{\text{Trs. Insp.}}$	.690	.773	.698	.783	.723	.808
Contour area at expiration	501 sq. cm.	479 sq. cm.	540 sq. cm.	535 sq. cm.	669 sq. cm.	611 sq. cm.
Contour area at inspiration	612 sq. cm.	587 sq. cm.	658 sq. cm.	646 sq. cm.	801 sq. cm.	734 sq. cm.
Contour expansion	111 sq. cm.	108 sq. cm.	118 sq. cm.	111 sq. cm.	133 sq. cm.	123 sq. cm.
Dorsoventral diameter at expiration	16.5 cm.	16.9 cm.	18.0 cm.	18.4 cm.	20.6 cm.	20.9 cm.
Dorsoventral diameter at inspiration	19.9 cm.	20.9 cm.	21.3 cm.	22.4 cm.	23.8 cm.	24.4 cm.
Dorsoventral expansion	3.4 cm.	4.0 cm.	3.3 cm.	4.0 cm.	3.2 cm.	3.5 cm.
Transverse diameter at expiration	26.3 cm.	25.0 cm.	27.5 cm.	26.5 cm.	28.9 cm.	27.3 cm.
Transverse diameter at inspiration	28.8 cm.	27.0 cm.	30.5 cm.	28.6 cm.	32.1 cm.	30.3 cm.
Transverse expansion	2.5 cm.	2.0 cm.	3.0 cm.	2.1 cm.	3.2 cm.	3.0 cm.
Lung capacity	3445 cu. cm.	3366 cu. cm.	3700 cu. cm.	3450 cu. cm.	4121 cu. cm.	3670 cu. cm.

The writer presents the following conclusions:

1. By means of the contour index chests may be divided into broad and deep, having low or high indices, respectively.
2. For broad chests the greater expansion is in the transverse diameter.
3. For deep chests the greater expansion is in the dorso-ventral diameter.
4. Broad chests have a greater cross-sectional area, both for inspiration and expiration, than deep chests.
5. Broad chests have a greater area expansion than deep chests.
6. Broad chests have a greater capacity (volume expansion) than do deep chests.
7. Broad chests having uniformly a greater capacity would seem to offer greater resistance to tuberculosis.

Nerve Physiology. The division of the sensory root of the Gasserian ganglion for relief of tic douloureux led to experiments by Frazier and Spiller[1] that are of physiologic importance. These consisted in cutting the nerve fibers in dogs and examining the structures several months later to see if regeneration of the sensory root occurred. The experiments indicate that no regeneration takes place. The statements of Van Gehuchten are cited in confirmation. Section of the large root of the trigeminus, though not an anatomic extirpation of the semilunar ganglion is equivalent to a physiologic extirpation, at the same time it does not destroy connection with peripheral organs. Recent anatomic studies in the territory innervated by the sensory root of the trigeminal nerve, show this territory is less than formerly supposed.

Circulatory Apparatus. *Blood Pressure and Pulse Rate.* Stephens[2] reports the results of observations on the influence of body position on the blood pressure and pulse rate. The data are readings from 22 male medical students by the Cook modification of Riva-Rocci sphygmomanometer. Each student was put through the standing, sitting, supine, head down, right lateral and left lateral

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(1) Jour. Amer. Med. Ass'n, Oct. 1, 1904.
(2) Ibid.

positions, allowing sufficient time to avoid errors. The accompanying pictures show the arrangement of subject, apparatus and the positions.

In discussing the effects on pulse rate, he says:

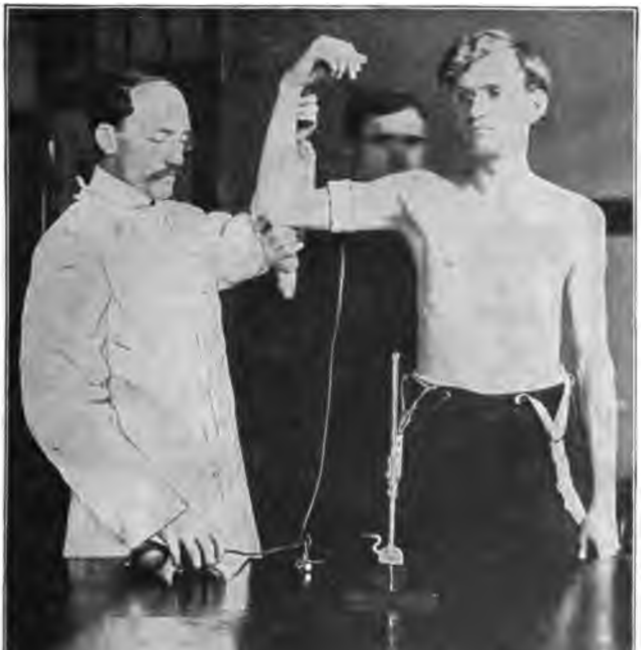

Fig. 12.

"The mere fact that the centripetal fibers which call the vagus into play by reflex action come chiefly from the heart itself, shows that one part, and a very important part, of the vagus function is to reduce the work done by the heart in the interest of the heart itself. We conclude, then, that the vagus acts as a protecting nerve to the heart, reducing the work thrown on that organ when, from fatigue or other causes, such relief is required by it. The fact, however, that there exist centripetal fibers which call the vagus center into activity, in such nerves as the sciatic and splanchnic, shows that the vagus mechanism may be called on to act in the interests of other parts of the body whose circulation requires to be diminished. We conclude, therefore, that the vagus may be used by other parts of the body to diminish the blood pressure and the output of the heart, and thereby reduce the circulation.

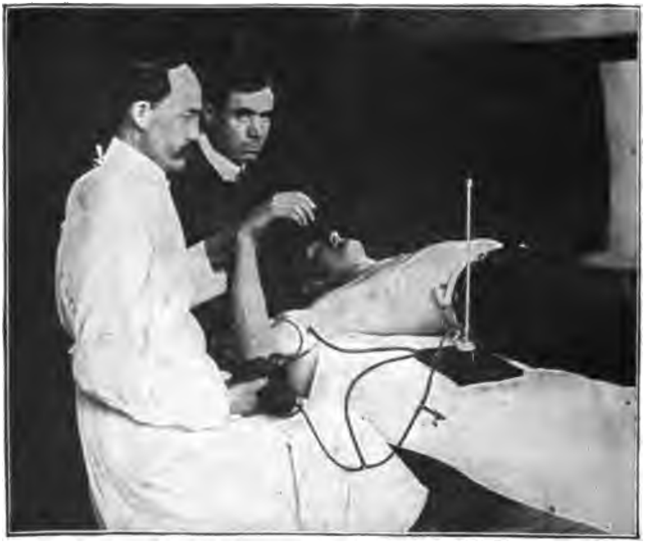

Fig. 13.

"Among the organs whose protection against over-congestion is of the greatest importance, it need hardly be said that the central nervous system takes the foremost place. It is well known that if the intracranial pressure be raised artificially, powerful excitation of the vagus center is produced. Vagus action also results from rise in the blood pressure in the systemic arteries, and the excitation thus produced can be shown to be due to the high pressure within the vessels of the central nervous system and not to any direct effect of the rise of pressure on the heart. We must, therefore, look on the vagus mechanism as a means by which the central nervous system gains protection against too great congestion.

"The dependence on the blood pressure of the degree of vagus action, and the readiness with which the vagus center in the medulla is called into play by a rise of the intracranial pressure, seem to us to indicate that the mechanism in question is especially employed in the interests of the central nervous system as well as the heart itself."

Now, if it be true that the vagus acts as a protecting nerve, both to the heart itself and the central nervous system, it is clear that the reduced heart rate in the various positions of the body in the order named is in response to the action of the vagus in endeavoring to protect the heart and central nervous system against the increasing pressure.

The experiments show that blood pressure increases in the brachial, from the standing to the head down position. The greater the hydrostatic pressure in the upper portions of the circulatory system, the greater the increase in pressure where the nervous and respiratory systems are normal. An increase in resistance is accompanied by increase in heart strength. The pulse rate decreases in the same order as blood pressure increases.

Mammalian Heart. MacWilliam[1] finds that spontaneous rhythmic contraction originates in the coronary veins and coronary sinus, as well as in the vena cava and pulmonary veins. Pulsations were observed in the anterior coronary vein as far down as the middle of the left ventricle. It was found that changes in blood pressure had very little influence on heart action when disconnected from the central nervous system. A range of variation from 1.6—6.6 inches mercury, aortic pressure showed it to be insensitive. This is quite contrary to what is seen during hemorrhage, etc., in the intact animal. The per-

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(1) Brit. Med. Jour., Sept. 24, 1904.

ipheral efficiency of the vagus was found to be little influenced by changes in pressure and asphyxical conditions. However, in the cat, admission of air into the lungs at certain stages of asphyxia, caused the heart to beat very rapidly, 340 per minute, even with the vagus in force.

New Functional Test of Heart. Katzenstein[1] proposes a test for the functional activity of the heart. When increased work is applied to the heart, blood pressure rises without increasing the pulse rate. The subject must remain quiet while pressure is applied to the iliac or femoral for 2 to 5 minutes. General blood pressure will raise .2—.6 inches of mercury, with the pulse rate unaltered. In any insufficiency the pressure falls and the pulse rate is increased. Where there is hypertrophy the blood pressure increases .6—1.6 inches of mercury.

Blood. Blood Glands. Williams[2] takes up the much argued question as to the functions of the *spleen.* This is an organ peculiar to the red blooded vertebrates, there being no analogous organ in the invertebrates. The connecting link between the two classes, namely, the amphioxus, whose blood is white, has no spleen. Therefore, it would be suggested that there is some connection between the spleen and red blood.

Bizzozero and Torre found that in the fishes all red blood cells were made in the spleen. They used only fresh specimens, treated with a watery solution of methylene blue to color the nuclei. Fish spleens were found filled with nucleated red cells, some of which were dividing. These nuclei they regarded as positive evidence that the red cells originated in the spleen. The inference is unassailable. Furthermore, since the bones of fish contain no marrow it is obvious that in this class of animals the spleen is the sole organ for the production of red cells. In the lower reptiles (the tailed amphibia) the same conditions prevail. The scanty amount of bone marrow in these animals is simple fat, containing no red cells, while the spleens are full of nucleated red cells.

In frogs, snakes and turtles the bone marrow begins to

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(1) Deutsch med. Woch., XXV, Nos. 22, 23.
(2) Amer. Med., June, 1905.

share with the spleen in the function of making red blood cells. In birds the function is divided between the bone marrow and spleen.

The author, by fixing common smears with a dilute solution of sublimate, salt, hemotoxylin-eosin, found the spleens of cattle and hogs to be full of nucleated red cells, many of them dividing. Artengo made similar observations on cats and dogs. Yet the evidence falls short of a positive demonstration that the spleen of vertebrates is the true organ for making of red blood cells.

Red bone marrow in the higher vertebrates also has this power. But marrow is a tissue, not an organ, deriving its blood making power from the embryonic mesoderm of which it is a remnant. In the embryo prior to formation of a spleen, the primitive mesoderm possesses the property of making blood cells. Later in embryonic life this is restricted to special organs and tissues. In adult life it is limited to the spleen in cold blooded animals, while in the warm blooded the red marrow continues throughout life to officiate as a subsidiary spleen. In this way nature provides for the added number of red corpuscles required by the higher animals for their increased respiratory activity and the maintenance of their body heat.

Internal Glandular Secretion. Cecca and Zappi[1] experimented upon some 18 pairs of rabbits, each pair taken from the same litter. In one of the animals, organs—as testes or ovaries—were removed and the other one was kept as a control. The effect of such removal on the general condition of the animal and specially on the thyroid, thymus, suprarenal and pituitary bodies are reported. It was found the castrated animal increased considerably in weight over its control mate. The thyroid was uniformly found to be increased in proportion to body weight in castrated rabbits. It contained more colloid matter in the vesicles, but without increase in the number of cells. In the suprarenals the medullary portion was hypertrophied, because of proliferation of epithelium. These cells apparently were normal. Examination of the thymus pituitary and parathyroid did not give evidence of change

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(1) Bull. del Sci. Med., March, 1904.

from normal. The writers consider that the reason for these variations is the inability of the thyroid to discharge its secretion into the circulation. In the suprarenals this is a possible connection with removal of sexual organs, because these structures are also developed from germinative epithelium.

Transfusion of Heterogeneous Blood. Salvioli[1] in transfusion experiments on dogs finds that living normal blood, plasma, serum and corpuscles are toxic for the dog. The main effect is that of reduction of blood pressure, cardiac and respiratory failure. Loss of coagulability is an important result, and takes place in conjunction with the toxic effect. The presence of hemolysins is demonstrated as existing in all parts of the blood, and not exclusively in the serum. Either this property is derived with great rapidity from the leucoctyes or it is normally present outside of this variety of cells.

The Significance of Leucocytes. Holmes[2] reaches the following conclusions regarding the lymphocyte: A gradual decrease in the small lymphocyte count is unfavorable. When repeated examinations give a low count an unfavorable prognosis is also indicated. A generally low count with an occasional higher count indicates a temporary effort towards convalescence. A gradual increase with an occasional low count indicates an uncertain convalescence. Poverty in small lymphocytes exists with great impairment in body nutrition and cell metabolism. It is not characteristic of any particular disease. When considered with the history of the case it has an important bearing as regards the probable outcome.

Myelocytes. Schindley[3] finds one may expect to see myelocytes in any condition where there is leucocytosis. These cells appear where the irritation has an action on the marrow causing a reaction. When they disappear along with the leucocytes they have no special significance. The writer reports that in some cases of malaria the blood findings are like pernicious anemia.

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(1) Arch. Ital. de Biol., 1904, p. 250.
(2) Jour. Amer. Med. Ass'n, Jan. 28, 1905.
(3) Zeit. f. Klin. Med., 1905, Nos. 5-6.

Ultra-Microscopic Examination of Blood and Secretions. Raehlman,[1] using Siedentropf's modified illumination, is able to see objects 1-5,000,000 of a millimeter in diameter. He describes in detail various optical illusions appearing in the field, which simulate membranes surrounding the ultra-microscopic particles, these pseudo-membranes even appearing to form cellular structure. He thinks it is not unlikely that the actively moving bodies found in the white corpuscles or serum even in a 1-10,000 dilution have a definite chemical composition and may be anti-bodies, thus furnishing a substantiation of Ehrlich's side chain theory.

Roentgen Rays. A report of the effect of Roentgen rays on the internal organs is made by Heineke,[2] who experimented on animals. He found there is a destructive process in the lymph follicles. The follicles of the spleen, mesentery and intestines of dogs were damaged by 15 minutes' exposure to a hard tube, placed near the abdominal wall. When two or three weeks were allowed to elapse before taking the specimens from the animals no changes were found, indicating the transitory nature of the lesions. It would seem that the action of the rays is not accompanied by a latent period, as is the case in skin exposures. It is apparently quicker, and the results indicate that the glands are sensitive. These experiments have a bearing on therapeutic applications.

Radium and Animal Tissues. Heinke[3] finds that radium has the same action on animal tissue as x-rays. The effect on lymphoid structures is not as severe as with the x-ray unless it is brought close to the surface. Such a close exposure is capable of inducing quite extensive degenerative changes even in a few hours' exposure.

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(1) Wiener med. Woch., 1905, No. 1.
(2) Muench. med. Woch., 1904, No. 18.
(3) Ibid., 1904, No. 3.

SECTION III.

PATHOLOGY.

Occult Blood in the Feces. Steele and Butt[1] point out the great necessity of having some more delicate test for blood in the feces than simple inspection, or ordinary microscopic examination. When blood can be seen with the unaided eye the evidence of intestinal hemorrhage can be determined by the pulse. For the detection of minute quantities of blood they make use of Klunge and Schaer's test:

Technic.—Thoroughly mix 5 grams of feces with enough distilled water to make semiliquid. Then thoroughly mix with an equal volume of ether, shake well, allow to stand for 15 minutes, and then pour off the supernatant liquid. Mix the residue with one-third its volume of glacial acetic acid and then add 10 c.c. of ether. Shake well, and allow it to stand for 15 minutes. The ethereal extract will rise to top as a clear liquid and can be poured off.

Take as much aloin as will go on the end of a spatula. Place in one-third of a test tube of 70 per cent alcohol.

To use; 2 to 3 c.c. of the clear yellow aloin solution is mixed in a test tube with the same amount of the ethereal acetic acid extract and 2 to 3 c.c. of ozonized turpentine is added and the whole gently shaken. The mixture should develop color in 15 minutes. If more time is given a color not due to blood will appear. The reaction may show in several ways: Either the whole mixture turns pink and then cherry red, or the aloin sinks to the bottom and forms a layer which gradually becomes a deep cherry red, or, if the aloin is allowed to flow gently down into the turpentine-ether-extract mixture a deep red ring is given.

The aloin solution must always be freshly made. The

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(1) American Journal Med Sciences, July, 1905.

ozonized oil is made by allowing a c.p. oil of turpentine to stand for at least 3 weeks.

Weber's test.[1] Shake a gram or so of gum guaiac in a test tube half full of ether, allow it to stand until it settles clear. Take 2 c.c. of the guaiac mixture and 2 c.c. of ether —acetic extract of feces and an equal quantity of hydrogen peroxid; shake well. The olive color quickly appears in the top portion. The guaiac must be freshly made.

Some of the shortcomings of these delicate tests are: A full meal of rare red meats will give it. Well cooked fish, fowl, ham or kidney will not give it. A diet of pressed beef juice will not give it. Vegetables will not disturb the aloin reaction. They sometimes make it difficult to judge the guaiac reaction. The taking of iron by the patient never interfered with the test. Care must be taken with regard to blood from innocent sources, *e. g.*, hemoptysis, epistaxis, hemorrhoids, fissures, menstruation, etc.

Kozickowsky (quoted by Steele and Butt) has demonstrated that these tests will show as little as 0.25 grams of blood in 2 grams of feces. Frank hemorrhages can usually be demonstrated by naked eye examination, or usually by the symptomatology without examination of the feces.

Other *recent literature* setting forth the value of the test is that of Boas and Kochman (Deut. med. Wochensch., 1901, No. 20; Archiv f. Verdauungskrankheiten, 1902); Boas (Deut. med. Woch., 1903, No. 43); Hartmann (Archiv f. Verdauungskrankheiten, 1904, Bd. X., No. 1), who reported on 1,000 tests; Joachim (Berlin, klin. Woch., May 2, 1904); Schunlinsky (Münch. med. Woch., 1903, No. 49; Schloss (Archiv f. Verdauung., 1904); Kozickowsky (Deut. med. Woch., 1904, No. 33; Petruchi (Zeitsch. für klin. Med., 1905), and Steele (Penna. State Med. Journal, February, 1905).

Steele and Butt have made 720 examinations, and have arrived at the following conclusions:

In ulcer of the stomach the presence of blood was inter-

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(1) **Berliner klin. Woch., 1898, No. 19.**

mittent. It was usually present one or two days in each week, and then subsequent to pain or vomiting.

Continuous bleeding usually means carcinoma. A milk diet or rectal feeding generally stopped occult blood in the feces. (It was their custom to keep their ulcer patients on rectal feeding until there had been no blood for a week.)

In cancer blood is not found until ulceration begins. It is usually continuously present thereafter. A source of error is the presence of blood in benign pyloric obstruction with stagnation. In cases without HCl and with no obstruction or stagnation, the presence of blood, according to Hartmann, is diagnostic of carcinoma.

Speaking as a whole the negative results of the test are of greater value in eliminating carcinoma than were the positive results in establishing it. It is also given in cirrhosis of the liver, purpura, tuberculous enteritis, and infrequently in typhoid (3 out of 19 cases by Steele and Butt, and 8 out of 18 by Petruchi).

Frequent examinations are necessary. Occult hemorrhage did not seem to precede visible hemorrhage in typhoid.

The test was always negative in hyperacidity, hypoacidity, mucous colitis, chronic gastritis, pernicious anemia, pneumonia, tuberculosis and a considerable number of other diseases.

Detection of Minute Traces of Sugar in the Urine. McEwen[1] believes that nearly all urines contain traces of sugar. His opinion is based upon experiments undertaken to explain the different crystals found in urine tested for sugar by the phenylhydrazin test. This test is applied as follows:

To 10 c.c. of urine in a test tube 1 gram of phenylhydrazin hydrochlorate and 2 grams of sodium acetate are added, the tube is kept at the boiling point for one hour. The tube is cooled, and the sediment is examined microscopically. The typical sugar crystals are delicate sulphur-yellow needles arranged in sheaves. In addition to these one usually finds "thorn apple" crystals. These McEwen determines to be due to minute traces of sugar.

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(1) American Journal Medical Sciences, June, 1905.

Rapid Paraffin Method (Lemke's method—personal communication). The following has been used for several years by Dr. Lemke, who gave it to Dr. Neff. The latter used it—exclusively—for 3 to 4 years with satisfactory results.

Dr. Schrager has employed it—exclusively—for 8 months with very satisfactory results.

The method consists in the following steps:

1. Small block of tissue in 95 per cent alcohol for 30 to 60 minutes.
2. Absolute alcohol, 40 to 60 minutes.
3. Benzol and toluol (equal parts), 40 to 80 minutes.
4. Paraffin (equal parts of soft and hard), for one hour (50° to 55°).
5. Imbed in hard paraffin.
6. Section.

The method takes from 3 to 4 hours, and very seldom fails.

Tissues of semi-solid consistency work best. The method is not very good for lipomata nor for fatty tissues in general.

An essential precaution with this method is that the tissues must be fresh—they should be in the hands of the pathologist within 2 hours after removal.

The blocks keep very well.

Benzol and toluol are not expensive.

A small quantity of the mixture can be used over and over for many tissues.

It is advisable to shake the bottle containing the tissue with benzol and toluol 2 or 3 times at intervals. (The clearing process is greatly accelerated by this, rather empirical, procedure.)

One knows exactly the time when the tissue must be transferred from benzuol and toluol to paraffin, by noting the beautifully transparent block.

Aceton as a Fixing Agent for Tissue. Henke and Zeller(1) say that aceton is a good fixing and hardening agent. It extracts water from the tissues, precipitates albuminous bodies and is soluble in paraffin. Technic of fixing, hardening and embedding:

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(1) Zentralblatt f. allg. Path. u. path. Anat., 1905.

1. Place the tissue in aceton, ½ to 1½ hours. When removed from the aceton the tissue should be as firm as tissue which has been fixed in 95 per cent alcohol.

2. Paraffin (125° to 132° F.), 1 hour. When placed in the warm paraffin the aceton evaporates.

The advantages are: It is probably simpler than any known method except freezing. Aceton is about as inexpensive as alcohol. If the water be extracted from the aceton it can be used over and over again. Dried copper sulphate can be advantageously used to extract the water from the aceton.

Schrager (personal communication) has had good results with this method. Its disadvantage is that the paraffin block is very prone to turn yellow and to shrink.

Scholz[1] modifies this method by combining with the celloidin method. The technic is as follows:

(a) Thin pieces of tissue, not exceeding 3 m.m., are put in *aceton* and kept at a temperature of 132° F. for ½ to hour. (The tissues may have been previously in formalin or alcohol.)

(b) Then the tissue is put directly in thin celloidin and kept at 98.6° to 104°, for 4 or 5 hours. (For curettements or granulation tissue it is advisable to keep the tissues for 15 minutes in alcohol-ether, before they are put in thin celloidin.)

(c) Add some thick celloidin.

(d) Transfer after 3 hours to thick celloidin.

(e) Keep the tissues for 12 to 14 hours under a glass cover, exposed to chloroform vapors.

(f) Weak alcohol for 2 to 3 hours.

The minimum time required is 21½ hours, the maximum 26.

Two precautions must be taken: *(a)* The tissue must be perfectly dehydrated. *(b)* The celloidin must be absolutely free of water. The author was able to cut sections only 8-10 *m.* thick. His method can be used for all tissues.

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(1) Deut. med. Wochenschrift, March 16, 1905.

Importance of Bacteriologic Examinatian of Cadavers. Simmonds[1] reported the results of bacteriologic examination of the heart's blood in 1,200 necropsies, made 12 to 36 hours after death. Streptococcus was found in 95 per cent. Some of the successful cases were: Scarlet fever, 88 cases; diphtheria, 38 cases; phthisis, 28; erysipelas, 25; phlebitis, 29; pyemia, septicemia, and malignant endocarditis, 38.

Canon[2] argues that examination of the heart's blood is liable to be misleading because of the bacteria that gain entrance from the usually infected viscera adjacent. With this view Gradwohl[3] agrees. He examined 50 cases, many shortly after death (2 hours), and all well refrigerated. In 78 per cent bacteria were found in the heart's blood. In only 3 cases were bacteria found in blood from the median basilic vein of the arm, but these were all cases of generalized pus infection and the bacterium was the same as that in the original atrium. On the other hand, the character of the bacteria in the heart's blood indicated accidental infection.

Fraenkel[4] makes a plea for *more frequent blood cultures* from post mortem material. He asserts that in a non-decomposed body cultures from the blood even as late as 70 hours after death can be presumed to have been present during life.

He also very strongly advises the routine use of Schottmüller's blood-agar medium, especially emphasizing its value in the diagnosis between Streptococcus pyogenes, S. viridis and S. mucosis. The last two cause a green discoloration of the surrounding media, but mucosis has a shiny consistency which differentiates it from viridis.

Excretion of Organic Phosphorus in the Urine in Certain Pathologic Conditions. Recent investigations indicate that these compounds may be present in the urine in considerable quantity and from systematic study of them probably some light on tissue metabolism may be given. Oer-

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(1) Virchow's Archiv., 1904, No. 3.
(2) Zentralblatt für all. Path., 1904, No. 4.
(3) Annales de l'Institut Pasteur, 1904, 767.
(4) Münch. med. Woch., 1905, No. 12.

tel[1] showed that a normal individual living on ordinary mixed diet excretes in the urine in twenty-four hours about 2 grams of total phosphorus expressed in terms of P_2O_5 and of this quantity about 0.05 grams exist in organic combination. Under normal conditions organic phosphorus constitutes about 2.5 per cent to 4 per cent of the total phosphorus excreted.

Symmers[2] found that in order for phosphorus determinations to be of value it was necessary to determine both the inorganic and the organic phosphorus as well as the total phosphorus and either of these determinations taken singly was liable to mislead. Furthermore, there was rhythm in the excretion of phosphorus independently of other considerations so it was necessary to continue the observations over some days. The proportion of organic P to total N excreted is 0.1 per cent to 0.5 per cent and there is normally a good deal of parallelism between these two substances—a parallelism which certain diseases serve to disturb. Diet and muscular exercise, contrary to the usual belief, made but little difference in the excretion of phosphorus. In various pathologic conditions 25 per cent to 50 per cent and sometimes 100 per cent of the phosphorus is in organic combination. In lymphatic leukemia there is a great increase in the excretion of organic P_2O_5. The ratio of nitrogen excretion to total P_2O_5 excretion and to inorganic P_2O_5 excretion remains about normal. In nervous diseases of the degenerative type the amount of organic P_2O_5 and the percentage of organic to total P_2O_5 showed an enormous increase. There does not seem to be the relation between phosphorus elimination and bone disease that is usually thought. For example, in osteomalacia no increase in phosphorus elimination was determined.

Two Forms of Amyloid Reaction. Referring to Neuman's study of the unreliability of the iodin-sulphuric acid test for amyloid, Davison[3] gives the result of four years' work. During this time only about one-half of the

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(1) Zeitschr. f. phys. Chem., XXVI, p. 123, and N. Y. Univ. Bullet. Med. Sc., 1901, Vol. I, No. IV, p. 165.
(2) Journal Pathology and Bacteriology, January, 1905.
(3) Muench. med. Woch., Feb. 15, 1905.

cases of amyloid infiltration reacted to the iodin-sulphuric acid test.

During this study he discovered there were two forms of amyloid material.[1] He believes there are two stages to the process and that the blue color with the iodin-sulphuric acid only occurs with the most marked cases. He reports a case of sarcoma of bone with many metastases, and marked amyloid infiltration of various organs.

Mast Cell Granules and Mucin. The similarity in behavior to polychrome methylen blue of mast cell granules and of mucin has been noted by Hoyer,Harris and others. Whether this resemblance was of importance, whether it meant kinship of origin, or whether it only existed on superficial observation is the question to which Clowes and Owen[2] addressed their inquiry, and first it was necessary to investigate the staining reagent. In 1901 Michaelis[3] had stated that in polychrome methylen blue the staining agent was methylen azure and that the blue had little part in the process, and that, contrary to the usual view, the product contained little or no methylen violet. Unna[4] studying polychrome blue anew disagrees with some of Michaelis' conclusions. He thinks the staining is due to azure and violet in a dilute potassium carbonate solution. Clowes and Owen are of the opinion that polychrome is more or less of an indicator and that the shade of color and even the color varies according to the reaction. Varying the fixing fluid and changing the reaction of the washes, the color of the stained elements can be varied at will, *e. g.,* a granule just now blue can be changed to a red by washing in an alkaline solution and vice versa back and forth indefinitely. They say that since mast cells take polychrome methylen blue much more readily than does mucin, and exhibit a blue color with acids and a red with alkalis, while mucin is red and decolorizes with alkalis, and also since the globules of mucin are far more soluble in alkaline solutions than are the mast cell granules it may

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(1) Virchow's Archiv., Bd. 155.
(2) Journal Med. Research, November, 1904.
(3) Centralblatt für Bak., etc., 1901, No. 19.
(4) Monatschefter für prakt. Dermatol., XXXVIII, No. 3, February, 1905.

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be considered that they differ very materially in chemical constitution.

Method of Staining Spirocheta pallida (of syphilis). Horand[1] gives the following method: Smear secretion on a slide. Dry. Or mix some secretion and some Hayem's solution. Smear. Dry. Fix in alcohol-ether or in absolute alcohol for at least 35 minutes. Stain with cherry red D. N. solution for one hour or more (cherry red D. N. 1, alcohol 10, water 1000). Wash in water. Dry. Mount in balsam.

The red cells will be rose, the leucocytes blue and the parasites red. Or, stain with Borrel (Practical Medicine Series, August, 1904, p. 47), or with that of Laveran (Practical Medicine Series, Ibid, 46), or with Horand's method (Presse Medicale, 1905), or Schaudinn's method, or with Bleu de Nil solution (Bleu de Nil, 1; alcohol, 10; water, 900).

Diagnostic Value of Tuberculin. It is questionable whether the discussion of tuberculin as a diagnostic agent finds a proper place in this book, yet the entire matter of methods is "grenzgebiete" or border line.

So many phases of the use of tuberculin are carried out in the laboratory, and so much of the work on the safety and reliability of this agent is now being done in the laboratories that we give it a place here. The writers have made such extended and satisfactory use of it for several years that we feel gratified at the favorable notice which it is receiving in the most authoritative quarters.

Trudeau, Baldwin and Kinghorn[2] found that experimentally produced corneal tuberculosis did not spread as the result of injections of tuberculin. On the contrary, as in previous observations, they noted some improvement in the foci. This observation has been recently confirmed by Gamble and Brown.[3] The observations on the specificity of the test by Trudeau, Baldwin and Kinghorn (loc. cit.) have been satisfactory. They conclude as the result of careful experimentation that the presence of tubercle bacilli or their substance in the tissue is necessary to a true

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(1) Lyon Medical, June 4, 1905.
(2) Journal Medical Research, August, 1904.
(3) Journal American Med. Assn., Oct. 21, 1905.

tuberculin reaction. Whereas enzymes such as trypsin or peptone sometimes produced a febrile reaction, it differed from the fairly uniform and regular reaction of tuberculin.

Furthermore, these experiments did not seem to indicate that the tuberculin reaction was an enzyme effect. They were not able to say just what part of the tubercle bacillus or its product was responsible for the reaction. The fat-extracted bacilli seemed to have more reacting substance than the others. They suggest that the reacting agent may be in the nuclein substance.

Baer and Kennard,[1] working from the practical standpoint, agree as to the specificity of the tuberculin reaction, and also, as to its safety. They say it is the best and most reliable agent for the diagnosis of incipient bone tuberculosis that they have seen. No harmful effects result from its use.

Further confirmation is that of Tinker (who reports observations on 400 cases) and many other clinical observers.

Against its use is ranged a large number of clinical observers. The inception of this opposition lay in the position of Virchow that the therapeutic use of tuberculin would cause degeneration of the embryonal tissues of the tuberculous nodule wall. That these tissues, which plug lymphatics, capillaries and tissue spaces, prevent the spread of the bacilli. Tuberculin would cause these cells to undergo necrosis and generalized tuberculosis would result. Knopf and other clinicians have seen tuberculosis generalize after the use of tuberculin. They do not claim there is any proof of relation except the fact that the two phenomena took place near together in point of time.

Trudeau, Baldwin and Kinghorn (loc. cit.) produced tuberculous lesions in the cornea. In this location the lesion could be kept under close observation. They were not able to see any phenomena tending to spread in or around these nodules as the result of the use of tuberculin.

Reed[2] examined 965 prison inmates with tuberculin. The

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(1) Johns Hopkins Hospital Bulletin, January, 1905.
(2) Journal American Med. Assn., Feb. 4, 1905.

subjects were detained under observation. He says that in no case did he find any ill effects. He was convinced of its value as a diagnostic agent.

Experiments with Tuberculins Made From Human and From Bovine Tubercle Bacilli. In this investigation Wolbach and Ernst[1] addressed their investigations toward two very important phases of the tuberculosis question, namely, the relation of bovine to human tuberculosis, and the curative action of tuberculin. The first of these was prominent, the second was rather incidental. Two cultures were made use of. One was from a human tuberculous testis, the other was from a nodule in the lung of a cow. The human bacillus was grown on human blood serum, the bovine on bovine serum. It will be noted that the bacilli were shielded from any possibility of influence from animal hosts other than those from which they were derived.

Testing the virulence of cultures grown under nearly similar circumstances, it was found that bovine bacilli were somewhat more virulent, *e. g.*, the average time required to kill guinea pigs inoculated subcutaneously was—with human bacilli—29 days; with bovine bacilli, 34 days. In rabbits the bovine-injected animal died in 3 months; the human-injected animal showed only local lesions at the end of 9 months; all animals lost weight after injection. The test of specificity of tuberculins was made as follows: Guinea pigs were inoculated intraperitoneally with 3 c.c. of a suspension of the density of a 24-hour culture of typhoid (Theobald Smith's standard). Tuberculin was used on the guinea pigs as soon as they began to lose weight. Approximately half the pigs were inoculated with human bacilli, and the other half with bovine bacilli. Half of each batch of pigs was then tested with human, and the other half with bovine tuberculin. There was no difference in the reactions given under any of the combinations. It was evident that if there is any difference in reaction it is not determinable by any known methods. There is no essential difference between the bacilli or their tuberculins. Wolbach and Ernst used tuberculins stronger than Koch (who said that .5 grams of tuberculin should

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(1) Journal Medical Research, October, 1904.

kill a guinea pig with tuberculosis of 4 weeks' standing in 6 to 36 hours).

Dönitz found that 15 German tuberculins averaged 0.1 to 0.3 grams as the lethal dose for a 400 gram guinea pig. About a week was usually allowed to elapse between the inoculation and the beginning of treatment. The initial dose of tuberculin was 0.012 to 0,016 grams, and the final one 0.2 to 0.32 grams. Injections were given three times a week. In one series 10 injections were given, in the other 50. The treated pigs lived longer than the controls, a fair number of them gained weight under the use of tuberculin while all of the controls lost weight. In addition to the improvement in general health the superficial lesions could be seen to improve, and in some instances heal completely in the treated pigs, whereas in the controls the lesions were always progressively .downward. The source, whether human or bovine, of the bacilli and of the tuberculins, did not seem to be of much importance.

De Schweinitz, Dorsett and Schroeder,[1] investigating the *comparative virulence of human and bovine tubercle* bacilli for some large animals, began by securing tubercle bacilli from 9 human subjects. They were not able to say with certainty how the subjects were infected, as complete observation, including necropsy, was possible in only a few cases. The major question was the possibility of infecting man with bovine tubercle bacilli. Therefore, to admit the possibility that the adults and children from whom the tubercle bacilli were derived were infected with bovine tubercle bacilli is to confess there is no question for solution, and that Koch was wrong in his position taken in 1901.[2] The bacilli from these human sources were used hypodermically and intravenously for the inoculation of calves, hogs and monkeys, and for infection by drenching and feeding, mixed in the food. Many secondary questions had to be taken into consideration, *e. g.*, human tubercle bacilli vary in virulence and animals vary much in their resisting power. After allowance for these elements they conclude that human and bovine tubercle bacilli are not

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(1) Bureau of Animal Industry, Bulletin No. 52.
(2) British Medical Journal, 1901, p. 189.

essentially dissimilar. It seemed that in the main the lesions produced by the bovine bacilli were more advanced and widespread than those by human bacilli, but the differences were only of degree, and were no greater than those between different cultures of bovine bacilli or different cultures of human bacilli. They say the differences are not specific nor even enough to permit the grouping of the bacteria as distinct varieties of the same species. The bovine bacilli are more pathogenic for ordinary domestic animals. This relatively summarizes the situation.

Spirocheta pallida in Syphilis. Schaudinn and Hoffman[1] succeeded in finding this spirillum in the secretions from many cases of syphilis. It was isolated in smears from the primary lesion, the papules, the glands and the spleen. The shape and the winding of the spirillum was distinctive, not at all like that of other spirilla. They demonstrated the same organisms in smears from experimental syphilis in monkeys. Metchnikoff, Roux and a considerable number of other observers[2] have verified this observation. Hoffman stained it with anilin water-gentian violet and with fuchsin, by leaving the specimens in the stain for 24 hours.

Buschke and Fischer[3] report finding the organism in a case of congenital syphilis.

Fraenkel[4] reports positive results in 6 cases. His method of staining was as follows: Fix 10 minutes in alcohol. Stain in Giemsa's solution (Grübler) 16 to 18 hours. Wash in water. Dry and mount in Canada balsam. The specimen must be examined with an oil immersion objective and a 4 to 8 eye piece. He thinks some of the reasons this organism has been overlooked are: The difficulty in staining; the high magnification required; the eye strain demanded, and the irregular distribution of the organisms.

Metchnikoff and Roux[5] prove that syphilis can be transmitted to anthropoid apes, gorillas, orangoutangs and chimpanzees. The lesions vary according to the source of the virus. They succeeded 10 times in 10 attempts. In-

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(1) Berlin. klin. Woch., May 29, 1905.
(2) La Bulletin Medicale. May 17, 1905.
(3) Deut. med. Woch., 1905, S. 791.
(4) Münch. med. Woch., June 13, 1905.
(5) Annales de l'Institut Pasteur, November, 1904.

oculations were made on the lids and around the genitals. The period of incubation was 22 to 37 days. The first lesion was a pale rose patch with shading edges. This then formed a central brownish scale. Next the mass became sharply indurated, then ulcerated. Then followed enlargement of the lymph glands. One month later secondaries appeared looking similar to—and distributed about as those of the human subject. Mucous patches appeared in the mouth, and secretion from these was used to inoculate other monkeys. In one case there was a paraplegia.

Becker and Mayer[1] and Arnal and Salmon[2] have found these experimental lesions are identical histologically with those of man.

In this study Metchnikoff and Roux were unable to find the parasite. (The positive results of their later studies have already been referred to.) They could not agree with Klingmuller and Bauermann[3] that the organism passes through a filter. The French experimenters took 2 chimpanzees and, using the same virus, but one portion filtered, the other not, got results proving that the microorganism is removed by filtration. They also demonstrated that 124° F. for 1 hour was sufficient to kill it. Glycerin was not destructive. Their search for a preventive virus was ineffectual. Many lower species of monkeys were inoculated with indifferent results. Of 3 attempts on rhesus monkeys one partially succeeded, though there were no secondaries and no adenopathies. They hope that judicious selection of these refractory species and inoculation thereof may yield a protective serum. (See also Annales Instit. Pasteur, 1903, p. 809, and 1904, p. 1.)

Lassar[4] has succeeded in inoculating a chimpanzee and has then used the lesion to inoculate a second.

Neisser[5] reviews the work of Metchnikoff and Roux and presents his own experiments. With rhesus monkeys he had no success. He succeeded with chimpanzees, orang outangs and gibbons. He concludes that the serum of a

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(1) Berlin. klin. Woch., 1905, S. 1,192.
(2) Annales Inst. Pasteur, 1904.
(3) Deut. med. Woch., 1904, S. 766.
(4) Berlin. klin. Woch., 1903, S. 1,189, and 1904, S. 801.
(5) Deut. med. Woch., XXX, 37, 38 and 39.

person having syphilis would neither transmit the disease to monkeys nor protect them against it.

In *Lyon Medical* for Feb. 21, 1904, Horand described a parasite which he thought was the cause of syphilis and which he called "hemoprotiste" of syphilis. He now[1] thinks it probable that the Spirocheta pallida is the same organism. He finds it in the secretion of chancres and in those of the various organs and fluids of the body. It is clear, hyaline, and its spiral makes at least 6 complete circles. Schaudinn and Hoffman speak of 14 circles sometimes occurring. The spirils sometimes taper. It is at least as long as the diameter of a red blood corpuscle. Occasionally one is 40 to 50 m. in length. Horand thinks he can identify a head, a body and a tail piece.

Nicholas Favre and Andre[2] also report finding Sp. pallida.

Surgical Scarlatina. Alice Hamilton[3] has collected 114 cases of so called "surgical" scarlatina to which she adds 10. Critically studying such records as exist she is convinced that some of them are drug rashes, and many are due to miscellaneous infections. Also, that the difference in symptomatology is dependent in the main upon the different causes of the disease reported. After these cases have been eliminated she thinks it probable that there are cases of true scarlet fever left, but the association with the surgical features is only an accident. She says "there is no convincing proof in literature," or, in her experience, that surgical scarlatina is anything more than scarlet fever in the wounded.

Experimental Measles. Hektoen[4] has carefully gone over the various reports of successful inoculation of measles, beginning with the report of Horne, of Edinburgh (1758). He concludes that none of these can be accepted. Judging from Ballantyne's report[5] of 20 cases of fetal measles, Hektoen concludes that the major etiologic factor in measles is in the blood. As no animals are

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(1) Lyon Medical, June 4, 1905.
(2) Lyon Medical, 1905, p. 1,366.
(3) American Journal Medical Sciences, July, 1904.
(4) Journal Infectious Diseases, February, 1905.
(5) Manual of Ante-Natal Pathology and Hygiene, p. 196.

susceptible to measles he injected blood from one man to another. He succeeded twice in producing measles. In the first experiment a boy of 9 had had scarlet fever. While recovering, and after having been free from fever for two weeks he broke out with a mild case of measles. On the fourth day of the fever 4 c.c. of blood were taken from a vein in the elbow under proper precautions, 2 flasks containing 50 c.c. of ascites broth (peptone broth, 2 parts; ascitic fluid heated to 131° F. for 54 minutes, 1 part) were inoculated with this fluid (1 c.c. in one, and 3 c.c. in the other). They were kept in the incubator for 24 hours at 98.6° F. At the end of this time both flasks appeared sterile.

Subcultures grown aerobically and anaerobically remained sterile; 4 c.c. of the first culture was mixed with 3 c.c. of blood and kept in the incubator for 24 hours at 98.6° F. and then was injected subcutaneously into a man just finishing desquamation after scarlet fever. On the thirteenth day his temperature rose to 103° and on the next day a measles rash appeared.

In the second case, 30 hours after the appearance of the rash in a typical case of measles, 10 c.c. of blood was drawn and placed in 4 flasks of bouillon. After 24 hours the flasks all seemed sterile; 5 c.c. from one of the flasks was injected subcutaneously into a man recovering from scarlet fever. On the 11th day fever rose and on the 13th day the temperature went to 103° F. and the eruption of measles appeared. All possibilities of accidental infection through contact or association, or through instruments were studiously avoided. The sterile appearing cultures showed that the infection was not due to ordinary bacterial contamination.

IMMUNITY.

It is necessary that the intelligent reader of the present day should have a general idea of the specific bodies, since —independently of all other considerations—these subjects are matters of constant allusion in all types of medical literature. The whole subject is new and was untouched in the curricula followed by most practicing physicians. To make matters worse, it has served to introduce a new vocabularly, many of the terms of which are not akin to any in general use. But on the other hand, they are of great clinical importance. Questions of normal function are being illumined and the hiatus between certain old causes and effects is being panoplied.

For example, Metchnikoff has told of phagocytosis and the destruction of bacteria that resulted therefrom, but this still left us to guess why leucocytes were attracted by bacteria, and how the bacteria ingested or approached were destroyed. We knew that the blood of a patient having typhoid would clump typhoid bacilli, but why? Likewise we knew that diphtheria was cured by diphtheria antitoxin, but how, and why? When diphtheria antitoxin first came into use it was hoped by many that treatment was now a matter of mathematics. But soon it was found that there was not uniformity of results. With the explanation of these discrepancies the study of antibodies has to do. Then there are physiologic questions such as secretion, its stimulation and automatic stopping, arrest of effort, etc. There are biologic questions such as the relation of species of animals to each other—all receiving some explanation from the study of antibodies.

It is true that the side chain theory of Ehrlich is purely a theory, and the lateral bond arrangement has no physical existence. But the same objection could be offered to the nebular hypothesis or, using a nearer parallel, the chemical ring schemes now recognized as basic in organic chemistry.

This theory is that cells are united to other cells or to organic chemical substances by a bonding factor termed a *receptor*. Unless a cell has receptors there will be no union. The cells or the substances will lie side by side without affecting each other. The capacity for influencing each other is capable of growth. A cell with a few receptors is liable to be stimulated by the substances bound by those receptors so that new receptors are formed. Let us say that the cell studied is a cell of some tissue, and the other body being considered is diphtheria toxin. Unless the cell has receptors the toxin does not poison it. If it has a few receptors the cell is moderately poisoned and new receptors are stimulated into existence. The toxic effect of the toxin is increased. Now the receptors can be so multiplied as that they drop away from the tissues and exist independently of them. Existing free they can still unite with toxin. Now let us say that 100 molecules of toxin get into the body, and 100 free receptors tie them up —none reaches the cells, no cells are poisoned. This is *immunity.* These free receptors are antitoxin substance. If we inject a horse with diphtheria toxin in small doses and so stimulate his cells to produce free receptors, then bleed him and inject his serum containing receptors into a diphtheria—poisoned child, we find the diphtheria toxins held away or pulled away from the child's tissue cells. We produce a *passive immunity.*

These specific bodies fall into three classes according to the structure of their receptors: For receptors are not simple structures. They are divided into two theoretic parts. A *haptophore* portion—which is purely a binding part, and a *toxophore,* or poisoning part. The term "poisoning" is used because the questions have been studied largely from that standpoint. But it must be remembered that the process is really a feeding. The result of the union may be nutrition and growth of the cell, or work, or injury, or destruction. In the first of the three groups belong the simple processes, such as antitoxin formation. The receptors have only haptophore portions. When a receptor unites with a molecule of toxin it binds its bonds but it may not even destroy the toxin, it certainly does not directly harm the bacillus producing the toxin.

There are other receptors which have a haptophore part and in addition a chemically active area called the toxophore portion. The receptors arose originally as feeding or protecting suckers or bulbs on the surface of body cells or of bacteria. When the number of receptors has become considerable they begin to drop away from the parent, and persist as free bodies. Through their haptophores they attach themselves to other structures; through their toxophores they exert their specific or *antiaction.* If the body is a toxin, and the toxins belong in the second group, one readily sees why the poisoning portion is called the toxophore. If the action is not toxic then some other term may be used, *e. g.,* "zymophore."

These bodies, in all three groups, are specific. The receptors of the one group do not fit any except very closely allied bodies. Hence the term "specific bodies" or *antibodies*—the term "anti" indicating that they are against or *vis a vis* to some other definite agency.

In the second group (having double portioned receptors) belong the agglutinins, the precipitins and the complements. The Widal test for typhoid fever is dependent upon agglutinins. The effect of typhoid poisoning continued for a few days is an increase in the number of receptors on the cells of the body. These receptors are stimulated into existence by typhotoxin, and in consequence they fit nothing except typhoid and—in much lesser measure—closely related bacilli. Presently the cells begin to shed these receptors into the plasma. They have two portions, a haptophore and a toxophore. In the Widal test the serum is mixed with typhoid bacilli. The bacilli are grasped by the haptophore portion, and so affected by the toxophore that they become nonmotile, shortened, rounded, and stick to each other, forming clumps.

The specific test for human blood is perhaps the most striking illustration of precipitins that can be offered. If a rabbit is repeatedly injected with human blood his tissues are stimulated to form receptors which fit human blood only. After the lapse of a little time the cells shed these receptors into the serum. Now when this rabbit's serum is mixed with human blood the receptors, through the haptophores, unite with certain chemical elements of the blood and the toxophores precipitate them.

It will be noticed that we have chosen three illustrations, each differing from the others.

The first illustration was toxin. These are usually bacterial products poisonous to most cells and the toxophore element is truly toxic. The second, the agglutinin, is a product of body cell activity and in the illustration used the cells agglutinated are bacteria. The toxophore portion is not toxic for the agglutinated bacteria are not killed. In the third illustration used the precipitins are produced by the body cells. No bacteria are concerned on either side of the equation. The toxophore portion is not, rightly speaking, *toxic.*

The third group becomes still more complex and difficult to understand. We have just seen how the body could neutralize (or rather shield itself from) a bacterial toxin, or how it could maim and cripple that bacterium by agglutinating it. It remains to be seen how the body destroys bacteria. For there are bactericidal or *antibacterial* bodies as well as *antitoxic* bodies. These are called "lytic bodies." We have seen that in the first group the receptor is a binding body only. In the second group it is both a binding and an actively modifying body. In the third we have a separate binding portion free in the tissues. It is called the amboceptor. In addition there is an actively modifying body, free also, usually called the complement. Now the specific body is not in existence until the complement locks up with the amboceptor to make one body. This combined body is the specific body. The cell, soaked in an immunizing agent called an antigen begets a double ended haptophorous body called an amboceptor.

Under the first two groups we noted that an ordinary receptor had a lock at one end, and when it broke away from the producing cell the other end was blunt. The receptor, of the third group, appears to be fastened to the producing cell at the middle, and to have a lock at each end. This breaks away and is a double ended bond—an amboceptor. One end of this haptophorous body—amboceptor—is to unite with the cell which is to be destroyed. This end is called the *cytophilous* haptophore. The other end is to unite with the lytic or cytotoxic body—the complement. This is called the *complementophilous* haptophore. When the complement and the amboceptor have united we have the antibody ready for action. The combined body unites by its cytophilous haptophore with the receptor of the cell which is to be destroyed and lysis results. The process is the same whether the cell which is destroyed is a bacterium or an animal cell. Sometimes the bacterium destroys the animal cell, sometimes the cell destroys the bacterium. Wherever the body itself produces its protecting receptors, amboceptors and complements the immunity produced is properly termed an *active immunity*. Wherever the substances are produced artificially and artificially introduced into another animal the immunity is *passive*.

Another phase of the question must not be lost sight of. The use of the antibodies in time leads to the production of anti-antibodies. For example, there may be an antiprecipitin, an antiagglutinin, etc. This antiagglutinin is a free receptor, and it may unite with the agglutinin, just as antitoxin unites with the toxin and in consequence no agglutination will occur. We have anticomplements, antiprecipitins, etc.

In the case of the more complicated processes, those of the third group, we may have antibodies which assume the function of either end of the haptophorous amboceptor leaving the other end free to bind.

We have antiamboceptors for the complementophilous haptophore and antiamboceptors for the cytophilous haptophore.

We must also bear in mind the fact that these antibodies are usually complex. There is a biologic difference between different portions of the body; for example, take a receptor of the second group—say a toxin. It is composed of a haptophorous and toxophorous portion. Now we can destroy or change the toxophorous portion so it loses its activity, and at the same time leave the haptophorous portion able to unite with the receptors of the cells. These modified toxins are called *toxoids* and sometimes paratoxins. They can be used to protect cells against toxins by occupying the receptors, or they can produce active immunity. This reads like vaccination. For the complements there may be anticomplements. These are similar in structure to antitoxins.

An excellent summary is that given in the article on "Immunity":[1]

1. The recognition of different types of tissue receptors by which peculiarities in the action of the different antibodies are explained. Receptors of the first order, as antitoxins, anticomplements and antiamboceptors, are re-

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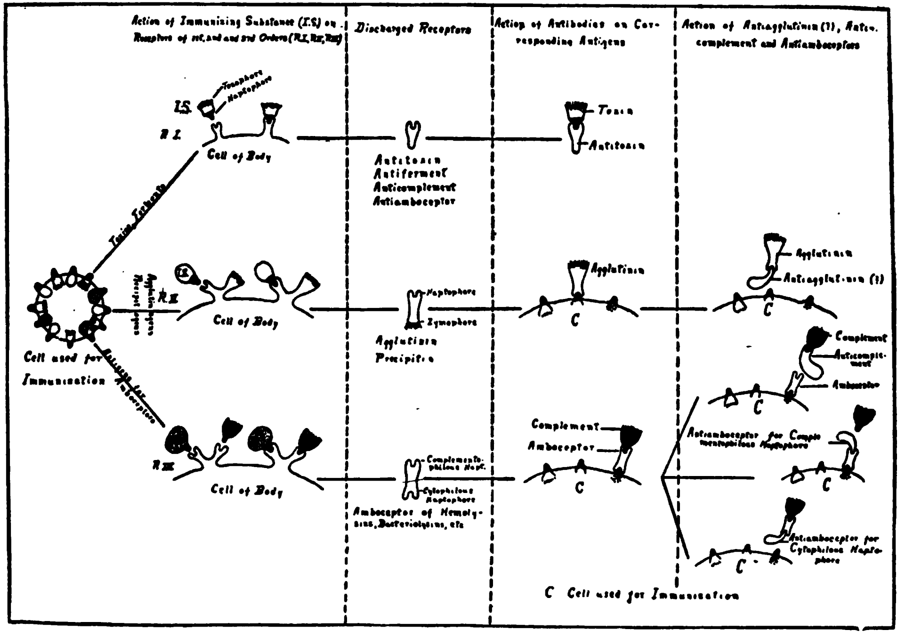
[1] Journal American Medical Association, June 24, 1905.

garded as relatively simple bodies because no other constituent can be recognized than the haptophorous group by which they combine with their homologous substances. Receptors of the second order are more complicated in that they have something more than the mere binding power; usually they are able to produce some observable change in the substance with which they unite. Hence, each has a toxophorous or a zymotoxic group in addition to the haptophorous, and the two groups are part of the same molecule. Toxins, agglutinins, precipitins and complements are receptors of the second order. Receptors of the third order, *i. e.,* the bacteriolytic, hemolytic and cytotoxic amboceptors, are still more complex in that they are, so to say, only partial antibodies, the complete body consisting of the amboceptor-complement complex. The amboceptor is not an active body, but serves as an intermediary body to connect the active substance, complement, with the cell. In the cytolytic process the amboceptor through its cytophilous haptophore first unites with the cell, and as a result acquires an increased affinity for complement, with which it unites through its complementophilous haptophore. Only after this double union is completed may complement affect the cell. From this it follows that complement in the cytolytic process does not combine with the cell directly.

Ehrlich has intimated his belief that the amboceptors play the chief rôle in the fixation of foods by the cells of the body.

2. The chemical theory explains the specificity which characterizes the formation and action of antibodies. Every antigen has a haptophore which is different from those of other antigens, consequently it unites only with the corresponding cell receptor, and the latter when overproduced and cast into the circulation retains its specific binding power for the corresponding antigen.

3. The multitude of antibodies which have been obtained indicate that the cells contain a vast number of different receptors which correspond to the three types now recognized; *i. e.,* there is a different antitoxin receptor for every kind of toxin, etc.


Action of Immunizing Substance (I.S.) on Receptors of 1st, 2nd and 3rd Orders (R.I, R.II, R.III)
Discharged Receptors
Action of Antibodies on Corresponding Antigens
Action of Antiagglutinin (?), Anticomplement and Antiamboceptors
I.S.
Toxophore
Haptophore
R.I.
Cell of Body
Toxins, Ferments
Antitoxin
Antiferment
Anticomplement
Antiamboceptor
Toxin
Antitoxin
Agglutinogens
Precipitogens
R.II
Cell of Body
Haptophore
Zymophore
Agglutinin
Precipitin
Agglutinin
C
Agglutinin
Antiagglutinin (?)
C
Cell used for Immunization
Antigens for Amboceptors
R.III
Cell of Body
Complementophilous Hapt.
Cytophilous Haptophore
Amboceptor of Hemolysins, Bacteriolysins, etc.
Complement
Amboceptor
C
Complement
Anticomplement
Amboceptor
C
Antiamboceptor for Complementophilous Haptophore
C
Antiamboceptor for Cytophilous Haptophore
C
C Cell used for Immunization

4. Ehrlich has limited the application of the term toxin to those substances of animal or plant origin, immunization with which causes the formation of specific antitoxins.

5. Receptors of the second order, toxins, agglutinins, precipitins and complements, undergo a peculiar degenerative change, spontaneously or as a result of exposure to injurious agents, in which the toxophorous or xymotoxic group disappears or is rendered inactive. The termination -oid is affixed to the altered bodies, as toxoid, agglutinoid, precipitoid and complementoid. Wechsberg has described a similar degeneration of one of the haptophores of amboceptors, calling the product amboceptoid. Toxoids and complementoids on immunization cause the formation of corresponding antitoxins and anticomplements, by virtue of retention of their haptophorous groups.

6. By means of a special technic devised for studying the neutralization of toxin by antitoxin—*i. e.,* the partial saturated method—Ehrlich found diphtheria toxin to be a very complex substance. Not all the molecules of the toxin have the same affinity for antitoxin, and according to the degrees of their affinity for antitoxin have received the names of prototoxin, deuterotoxin and tritotoxin. Similarly, protoxoids and syntoxoids are molecules of toxoid having different affinities for antitoxin.

7. It is thought the incubation period which characterizes the action of toxins represents to a large degree the time required for the action of the toxophorous group after the toxin has been bound by the cells.

8. Ehrlich claims that the diphtheria bacillus secretes two toxins, one of which causes the acute manifestations of diphtheritic intoxication, whereas the second toxin—*i. e.,* toxon—has a prolonged incubation period and probably causes diphtheritic paralysis. Toxon has a lower affinity for diphtheria antitoxin than the other constituents of the toxin solution, but is neutralized by the same antitoxin. This view is strongly opposed by Arrhenius and Madsen, who, working on the basis that the neutralization of toxin takes place according to certain laws of physical chemistry, claim that toxon is nothing more than toxin which has dissociated from the toxin-antitoxin molecule.

9. Ehrlich stands for the multiplicity of complements in opposition to Bordet and others who claim the existence of but one alexin. The various complements differ in the nature of their haptophores, without regard to possible differences in their zymotoxic groups.

10. Only those organs which have suitable receptors may produce an antibody for a given antigen—*i. e.,* only those cells which may enter into chemical combination with the antigen. It does not follow, however, that only those organs which show clinical or anatomic lesions may produce, say, an antitoxin; for other organs not so susceptible to the action of the toxin may still possess the suitable receptors and cast them out as antitoxin.

The various types of immunity are explainable on the basis of the side-chain theory in the following terms:

1. Natural antitoxic immunity may depend on (*a*) a lack of suitable cell receptors, the toxin consequently finding no point of attack; or (*b*) on the presence of natural antitoxins.

2. Acquired active antitoxic immunity depends on the multiplication and excretion of cell receptors (antitoxin) into the circulation, the new formed bodies having the power of combining chemically with additional toxin which may be introduced.

3. Passive antitoxin immunity, as established by the injection of an antitoxin, depends on the ability of the antitoxin to combine chemically with the toxin and thus to divert the latter from the cells.

4. Natural antibacterial immunity depends on (*a*) a lack of suitable cell receptors with which the toxic bacterial constituents might combine, or (*b*) on the presence of natural bacteriolysins (amboceptors and complements).

5. Acquired active antibacterial immunity depends on the multiplication and excretion into the circulation of specific cell receptors (amboceptors) which have the power of uniting with complement to kill the micro-organisms which may be introduced.

6. Passive antibacterial immunity, as established by the injection of a bacteriolytic serum depends on the ability of the amboceptors contained in the serum to unite chem-

ically with the receptors of the micro-organism, as a result of which complement is absorbed to kill and perhaps to dissolve the bacteria. The complement may be present in the serum which is injected, or the natural complement of the individual may be utilized by the amboceptors.

Discussion of Immunity.[1] Before the Section of Pathology of the British Medical Association a noteworthy discussion of immunity took place. Ritchie opened the discussion. A few years ago the subject had three main points at issue: (1) Natural immunity in relation to disease; (2) artificially acquired immunity; (3) the relation of these conditions to recovery. More recently the requirements of therapeutics and the development of high degrees of immunity, such as are never seen naturally, has drawn observers away from the main propositions. The basis of fact regarding immunity today has in it the recognition of bacterial poisons and their property of becoming fixed to susceptible cells when injected. The entire matter is now accepted as being one of chemical union-neutralization, obeying chemical laws, and that the combinations can be dissociated within certain limits. Other pathogenic bacteria do not produce toxins, and in the case of these the bacterial cell itself must be destroyed. There are two substances in the immune animal that have to do with the killing of bacteria—one, known as complement (thermolabile), exists normally in more or less amount, and the other immune body (thermostabile), which is either absent or present in small amount in normal serum. During the progress of immunization the immune body can be found in large quantity and is specific for the protoplasm which stimulated it; but, on the other hand, the complement is very little influenced. Bacteriolysis, or disintegration of the invading bacterial cell, sets free the intracellular toxins, and may in itself cause a much more severe poisonous effect to be observed in the highly immunized animal. Lysis in all of its phases becomes a very important subject in relation to immunity against the bacterial cell.

In speaking of recent work, Ritchie called attention to the investigation of Meyer and Ransome, who have established that tetanus toxin reaches the nerve cells by way of the motor axones. Further, they have shown that the injection of antitoxin will not necessarily save an animal from later injections of toxin if these are made into motor nerves. The view taken is that the antitoxin can only reach the cells by the roundabout way of the lymphatics. This failure of protection by antitoxin would also tend to disprove Ehrlich's theory that tetanus antitoxin was largely formed in the nerves.

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(1) Brit. Med. Jour., Sept. 10, 1904.

Another work of interest is that of Muir, who has shown that it is possible to dissociate a certain amount of immune body from saturated corpuscles and cause it to become attached to fresh corpuscles. The deduction is that an exchange of molecules can take place between cells when they are merely in contact. He also established that this relationship was quantitative, therein opposing the French school. The complement does not dissociate in this way, nor does it appear that the immune body is changed in any way by its temporary attachment to the cells.

The investigations of Wright and Douglas on the ingestion of bacteria by cells are far-reaching. Some bacteria are killed extracellularly, while others are not injured by serum but are destroyed by phagocytosis. There is, moreover, a previous sensitization of the cells, before ingestion, by union with a substance existing in the plasma. This body has been named "opsonin" by the writers. Whence this substance is derived is as yet unknown.

Dreyer discussed the nature of agglutination. The present view is that it is due to the combination of three elements: An agglutinable substance in the cells, agglutinin in the specific serum and salt. As a result of his experiments he does not find the relation of agglutinin and toxin in B. coli is such that when increased amounts of agglutinin are added to the same amount of bacterial cell the ratio of absorption falls, as reported by Eisenberg and Volk. His results show that the absolute amount absorbed under these circumstances increases with the increased amount of agglutinin applied, but that the ratio of amount originally present and amount absorbed remains practically constant.

The result of applying heat to agglutinable substances. When, for instance a B. coli emulsion is heated to 140° F. for a time agglutinability is decreased or lost. Dreyer does not think this is due to destruction of agglutinable substances, because he was able to show that by prolonged heating (even for thirteen hours at 212° F.) the agglutination phenomena returned, and even persisted this length of time. It would seem that heating for two or three hours at 212° gave the highest relative agglutination test.

The effect of acids and alkalies was studied by Dreyer, and his reports confirm the work of others. The usual result has been that large amounts of acid inhibit agglutination, while small amounts increase it. His experiments show that very different results would be obtained if serum or saline solutions were used. With saline solutions acidification had no effect, while with acid serum the agglutination phenomenon was increased. Alkalies were found to inhibit or even destroy agglutination.

Madsen presented his views on the chemistry of toxin and antitoxin. His theory differs from that of Ehrlich in that he considers these bodies as having a much less complicated structure and that their combining activities are subject to mathematic determination, as is the case in chemical reactions—*e. g.,* diphtheria antitoxin and toxin do not neutralize so as to give just the results one might expect from the measured amounts taken. The reaction follows a ratio so that curves showing the manner and extent of counteraction may be plotted. If 100 minimal lethal doses of toxin are taken and mixed with antitoxin in amount of fractions of 1 unit the result in the number of *m. l. d.* doses remaining is shown in the table. Beside this are the calculated number of *m. l. d.* as determined by Madsen:

Antitoxin fraction of antitoxic unit.	Toxin. Number m. l. d. observed.	Remaining calculated.
0	100	100
0.1	75.1	75.1
0.15	62.6	62.7
0.2	47.6	50.6
0.25	45.8	38.6
0.3	25.9	27.3
0.35	17.3	17.5
0.4	9.6	9.9
0.45	5.3	6.0
0.5	3.1	4.1
0.6	1.6	2.6

Martin discussed snake venoms. What we now know of their poisons indicates they are proteid solutions, from which the toxic principle cannot be separated by the chemical means now at hand. By biologic experiments they are known to contain substances having the following properties (not necessarily all present in the same venom):

1. A powerful fibrin ferment.
2. A neurotoxin, with—in many cases—an affinity for the cells of the respiratory center.
3. A neurotoxin, with an affinity for nerve endings in muscles and especially in the diaphragm.
4. Various cytolysins; *e. g.,* that which destroys red blood cells, endothelium of blood vessels, leucocytes, nerve cells, etc. (Nature of amboceptors.)
5. An antibactericidal body (of the nature of an anticomplement).
6. An antifibrin ferment.
7. Agglutinin for red blood corpuscles.
8. A proteolytic ferment.
9. A substance which causes systolic arrest of the isolated heart.

In speaking of the action of antitoxin he reports some observations showing that time is a very important factor in the results which may be expected. When fifteen to thirty minutes' contact between the venom and antitoxin is allowed to take place, what would be a fatal result in two to ten minutes is avoided. The same takes place in a degree when large or small amounts of toxin are mixed with the same amount of antitoxin.

Noguchi reported experiments with antivenines. He concludes that their action is highly if not strictly specific both *in vitro* and *in vivo;* therefore, only the specific antivenine must be used in the treatment of venin poisoning. The relation between the antitoxic and antihemolytic powers of an antivenin is quite variable. The strength of one cannot be estimated by determining the other constituents. The anticrotalus and antimoccasin serums possess a very great therapeutic value.

The enormous volume of work on susceptibility and immunity that has been done during the past year has followed in the main one of two lines: (1) Investigation of the chemic and biologic peculiarities of the better known specific substances; (2) morrfectious of technical procedures.

In the first group is the study of *opsonins* and their relation to phagocytosis by Hektoen and Ruediger.[1]

Studying the minutiæ of phagocytosis Wright and Douglas[2] describe certain phenomena of phagocytosis due to chemic substances inherent in the plasma called opsonins. These bodies existing in blood serum are taken up by bacteria, whereupon those bacteria are ingested and destroyed by phagocytes—phagocytosis.

The relation of these bodies to phagocytosis, and therefore to infectious diseases, can readily be understood. Elaborate studies of the properties of this theoretic group of bodies or capacities of serum (or potentialities) have been made by Wright and Douglas, and Hektoen and Ruediger. Opsonins are thermolabile, being destroyed by heating serum to 136-140° F. They have two groups of bonds—haptophorous and opsoniferous. By heating bacteria that have been sensitized the opsoniferous group are destroyed, but the haptophores hold on to the bacteria, so there are no amboceptors vacant and the bacteria cannot be resensitized.

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(1) Journal Infectious Diseases, January, 1905.

(2) Proceedings Royal Society, 1903, p. 357, and 1904, p. 128, and Lancet, Oct. 22, 1904, p. 1,138.

"Sensitizing" is a term suggested by Hektoen and Ruediger. Bacteria for which certain phagocytes have no affinity can be treated with serum from a different source (sometimes from a different animal), whereupon phagocytosis occurs. This Hektoen and Ruediger term sensitizing.

The method of estimating phagocytosis was that of Leishman,[1] namely, mixing bacteria with a leucocyte containing fluid and putting the mixture in an incubator at 98.6° F. for one hour, then staining films made from the fluid with Leishman's stain. The bacteria in the leucocytes are then counted. At least twenty counts should be averaged. Certain bacilli did not make satisfactory tests; *e. g.*, the leucocytes would contain so many anthrax bacilli that counting was not possible, or typhoid bacilli showed such a disposition to break up that counting was not very accurate.

Very interesting was their observation that certain substances as formalin, $Ca\ Cl_2$, $Ba\ Cl_2$, $Sr\ Cl_2$, $Mg\ Cl_2$, K_2, So_4, $Na\ HCo_3$, $Na_3\ C_6\ H_5\ O_7$, $Na_2\ C_2\ O_4$, $K_4\ Fe\ (CH)_6$, bound the opsonins so that they could not act on bacteria. They were antiphagocytic. Various writers have offered additional evidence tending to show the stimulation of phagocytosis by opsonins.

The Practical Importance of the Local Immunity of Tissues. As is well known, certain bacteria are tolerated by various tissues, whereas were they present in other localities they would produce grave pathologic changes. One has only to recall the relatively great tolerance of the gastro-intestinal mucosa for bacteria as compared with the marked susceptibility of the serosa of the closed cavities, or the fact that B. coli is a harmless saphrophyte in the intestines of adults, while the same organism in the urogenital tract produces the most severe inflammation.

The explanation of these facts is the subject of an article by Wasserman and Citron.[2] They point out that those tissues which from the beginning are sterile and shielded from contact with bacteria are the most susceptible, *e. g.*, the peritoneum, pleura and pia-arachnoid, while those

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(1) British Med. Journal, Jan. 11, 1902, p. 73.
(2) Deutsch. med. Woch., 1905, No. 15.

which come in most intimate contact with bacteria are the most tolerant, the best example being the gastro-intestinal mucosa.

This would lead one to suppose that continued contact with bacteria produces a local immunity of the tissue. This supposition becomes the more probable when we see that with increasing age certain tissues increase in resistance; *e. g.,* in calves B. coli is very infectious and produces a severe dysentery, while the same organism is harmless in the adult animal. The same holds good of man, for it has been shown by Heubner, Escherich and others that B. coli plays a different rôle in infants from that in adults.

To prove this immunity is local rather than general the authors injected B. typhosus into the peritoneal and pleural cavities and intravenously. They found the pleural and peritoneal exudates were much more bactericidal than the blood serum.

It is well known that many persons who are more or less constantly exposed to typhoid infection and from whose stools typhoid bacilli may be isolated are perfectly well. We explain this by saying that they have acquired more or less immunity. The authors claim this immunity is due to some local change in the epithelial cells of the intestine, and not to the presence of antibodies, for were the latter the case the serum would show increased bactericidal or agglutination properties, which it does not. That this immunity is not due to lessened virulence of the organism is shown by the spread of the infection to other persons. The same holds true in regard to cholera, dysentery and various other diseases.

We must distinguish between experimental and spontaneous infection. As Theobald Smith pointed out before the International Congress at St. Louis, there is no direct relation between the virulence of a micro-organism for a species of animal in experiment and the ability of the same organism to cause a spontaneous epidemic in the same species. This is well shown by the marked susceptibility of the mouse to experimental *Schweinseuch,* while a spontaneous epidemic of this disease is unknown in mice. This latter fact is due probably to a local immunity of the cells at the atria of infection.

Permanent immunization against an organism capable of producing a spontaneous infection in an animal is possible only by introducing living organisms and never by the use of dead ones. For instance, we have such artificial immunities as those of cattle to tuberculosis; sheep and cattle to anthrax; swine to swine erysipelas and Schweinseuch; man to smallpox and hydrophobia, and rats to plague, all produced by the use of attenuated living organisms.

This permanent immunity is to be sharply distinguished from the temporary immunity produced by the use of dead organisms.

While *antibodies are essentially specific,* specificity is not absolute. This phase of the question is the subject of researches by Pearce[1] bearing particularly upon the specificity of somato-genetic cytotoxins. He says that the cells of the various organs of the body, while differing in morphology and function, have certain receptor characteristics in common, and one type of cell may therefore produce antibodies affecting several cells of different morphologies, but like receptor groups. Specificity is due to peculiarities of receptors and not of cells. Pearce thinks that some errors have arisen because the tissues made use of for experimentation have not been washed free from blood and other juices and some properties of those fluids have been ascribed to the cells. He continues the exploitation of this idea in an article on *Experimental Production of Liver Necrosis by Intravenous Injections of Hemagglutinins.*[2] The focal necroses found in the liver in various diseases may be due to several factors. They may be due to cytotoxins. Pearce thinks many of them are due to hyaline thrombi, resulting from hemagglutinins. This opinion is confirmed in varying degree by Flexner, Boxmeyer and by Ziegler. That the necroses were found only in the liver is due to the slower circulation and the smaller vessels of that viscus. That they are found in the superficial zones is also capable of mechanical explanation. Pearce believes it is possible that many of the bacterial poisons are both hemolytic and hemagglutinic and these are responsible for hyaline thrombi composed of red blood cells. These cause necrosis from starvation.

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[1] (1) Journal Medical Research, July, 1904.

[2] (2) Ibid., October, 1904.

Power of Liver to Destroy Diphtheria Toxin. Brimton and Bokenham[1] quote Fraser as having found that the bile of animals rendered immune to snake venom contained an antitoxin. Combining this with the knowledge that in making diphtheria antitoxin it has been noted that the same horse will give sera of different strength in different days, they conclude that immunity—natural or acquired—is nothing more than an extension to the cells of the tissues generally of a power which is constantly exercised during digestion by those of the intestines and liver.

A series of experiments showed them that diphtheria toxin slowly injected into the veins which pass through the liver is much diminished in virulence. This is not due to admixture with blood but to action of the liver cells. Nucleo-proteids extracted from a liver thus subjected to injection have marked antitoxic properties. Bile and juice expressed from such livers have slight antitoxic powers. The protective power of the liver seemed great. Toxin passed through the liver was only one-fifteenth as lethal as before it was injected. They were certain that the diminished virulence was not due to dilution. [The efforts at locating the element in which this effect is consummated do not appear satisfactory to the Editor.]

DISEASES SOMETIMES ASCRIBED TO ANIMAL PARASITES.

Yellow Fever. As we near the close of the heated term of 1905 we find yellow fever well in hand in the Southern States. In New Orleans the control of the situation is excellent. The mosquito theory has been the basis of action, and in consequence there has been an epidemic history unparalleled for that city. Throughout the adjacent country control has not been so scientific in the main, and the consequences have been more baneful. All in all, the country and science have a right to congratulation. The following

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(1) Journal of Pathology and Bacteriology, November, 1905.

circular was issued by the Public Health and Marine Hospital Service July 31, 1905:[1]

"NO MOSQUITOES, NO YELLOW FEVER.

"The infection of yellow fever is carried by mosquitoes, and by no other means is the infection spread.

"Persons take the disease by being bitten by mosquitoes that have previously bitten a yellow fever patient.

"The mosquitoes to become infected must bite a yellow fever patient during the first three days of his attack. These first three days, therefore, are the most important time for preventing the access of mosquitoes to a fever patient.

"It is often difficult to decide during the first three days whether a patient has yellow fever; hence the necessity in threatened communities of placing a mosquito bar immediately around every patient who has fever of any kind, and for three days at least.

"FACTS ABOUT SCREENING.

"1. The netting used should have meshes fine enough to prevent the passage of mosquitoes (at least 18 to 20 meshes to the inch).

"2. It is important to screen the windows and doors of the house. It is doubly important to screen the beds of fever patients.

"3. Mosquitoes can bite through mosquito nets when any part of the patient's body is in contact with the netting.

"4. Frequent examinations should be made to see that there are no torn places in the netting or that no mosquitoes have found a lodging inside.

"5. The netting should be well tucked in to keep mosquitoes from entering.

"6. If mosquitoes are found within the netting they should be killed inside and not merely driven or shaken out.

"7. All cases of fever should be promptly reported to the local health officer. Awaiting his arrival they should be covered with a mosquito bar.

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(1) Jour. Amer. Med. Assn., Aug. 12, 1905.

"FACTS BEARING ON MOSQUITO DESTRUCTION.

"1. Mosquitoes live in the vicinity in which they breed. They do not often fly a long distance.

"2. Mosquitoes breed only in water—usually in artificial collections of fresh water.

"3. The young mosquito, or wriggler, lives in water at least seven to twelve days.

"4. Although the wrigglers live in water, they must come frequently to the surface to breathe.

"5. Coal oil on the surface of the water prevents the wrigglers from breeding.

"6. Destroy the breeding places and you will destroy the mosquitoes.

"7. Empty the water from all tubs, buckets, cans, flower pots, vases once every forty-eight hours.

"8. Fill or drain all pools, ditches, unfilled postholes, and the like.

"9. Change regularly every day all water needed in chicken coops, kennels, etc.

"10. Treat with oil all standing water which cannot be screened or drained (1 ounce of oil will cover 15 square feet of surface). The oil does not affect the water for use if the water is drawn from below.

"11. Where oil is applied to standing water it must be distributed evenly over the surface.

"12. Put fine wire netting over cisterns, wells and tanks of water in everyday use.

"13. Places in which it is undesirable to put oil, such as watering troughs for stock, lily ponds, and so forth, can be kept free from wrigglers by putting in gold fish or minnows.

"14. Clean away all weeds, grass and bushes about ditches, ponds and other possible breeding places, since these afford a hiding place for the mosquitoes.

"15. Clean up vacant lots and back yards of all cans, tins, bottles and rubbish.

"16. First do away with, or treat, all places where mosquitoes are known to breed, and then begin to work on places where they might breed.

"17. Inspect and treat with coal oil, gutters, culverts, ditches, manholes, catch basins, etc., along the roadside. Manhole covers should be screened.

"18. Houses should be cleared of mosquitoes by burning 1 pound of insect powder or 2 pounds of sulphur to 1,000 cubic feet of space. The mosquitoes will fall to the floor and should be collected and burned.

"19. Success in mosquito destruction depends on the co-operation of the members of the entire community.

"20. While the infection of yellow fever is carried by a single species of mosquito (the *Stegomyia*), to insure its destruction it is necessary to destroy all mosquitoes.

"In places liable to yellow fever both individuals and communities have an effective method of protecting themselves, as indicated above. Use the mosquito bar at once over all cases of fever until the danger from yellow fever has passed. Destroy all mosquitoes."

Preliminary Report on Cells Found in Yellow Fever Blood With Reference to Their Etiologic and Diagnostic Significance. Pothier, Hume, Watson and Couret[1] say that careful study of the blood of yellow fever patients has shown the presence of certain cells which can also be demonstrated in the stomach of a recently infected *Stegomyia*. They are extra cellular, and are single or in small clumps. They vary in size from twice the size of a pneumococcus to one-fourth the size of a red blood cell. They are round to ovoid in shape. They are encapsulated and show a highly granular protoplasm surrounding a nucleus containing one or more chromatin granules. They describe four types, as shown in the illustrations. They were only found on the fourth day of fever. Fresh blood and cerebrospinal fluid gave negative results. They recommend that the smears be fixed in wood alcohol for two minutes. Dried in the air. Stained with Delafield's hematoxylin for three minutes, acid alcohol until reddish brown, ammonia water till blue. Wash in water. Stain for 15 minutes in 1-1000 aqueous solution of eosin. Dry. Clear with clove oil. Mount in balsam.

Fifty-two slides were examined with 49 positive results. They were not found in the blood of other patients.

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(1) Journal Amer. Med. Assn., Sept. 23, 1905.

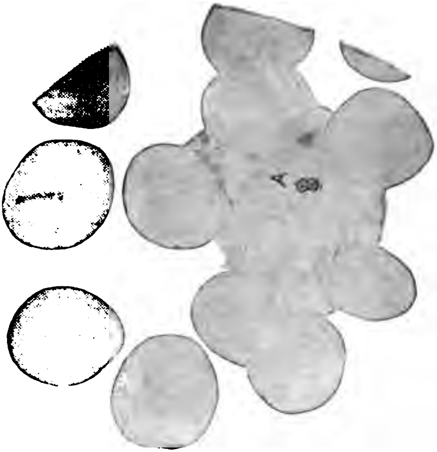

Fig. 1. Type A. Young form, surrounded by a pseudocapsule. (×1300.)

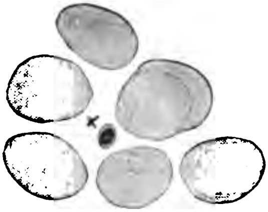

Fig. 2. Type B. Well marked nucleus, chromatin granules, narrow rim of protoplasm. (×850.)

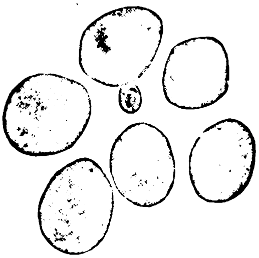

Fig. 4. Type C. Deep staining nucleus, narrow rim of protoplasm, definite capsule. (×850.)

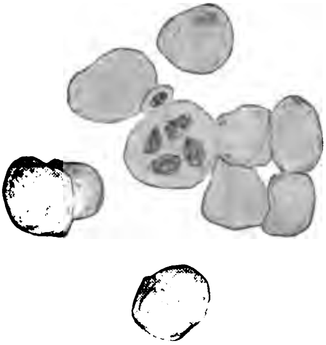

Fig. 3. Type B. Slightly older form than Fig. 2. (×900.)

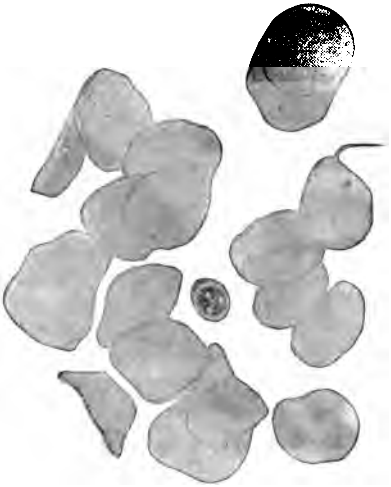

Fig. 5. Type C. (×1300.)

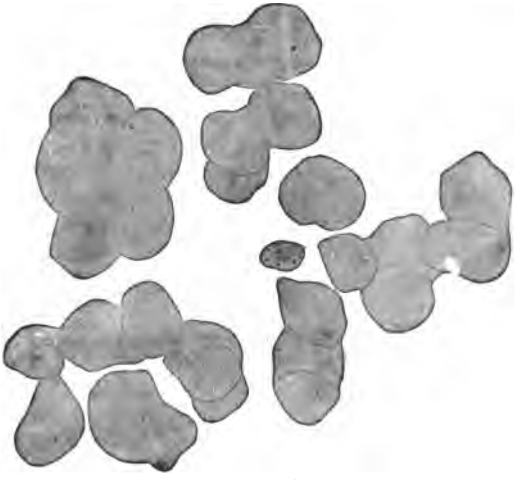

Fig. 6. Type D. (×850.)

The public press announces that Dr. Archinard has also succeded in discovering a protozoan body in yellow fever blood.

Etiology of Variola. Howard and Perkins[1] say that all efforts to demonstrate bacteria in smallpox have failed, as have all efforts to grow ultra microscopic forms from variola material. Park has shown that variola fluids do not transmit the disease after having been passed through a Berkefeld filter. Moved by these considerations they have investigated the protozoan bodies in smallpox and conclude that the bodies described by Councilman and his coworkers represent stages in the life cycle of a protozoan parasite. They were able to confirm all of the observations of Calkins[2] except the invasion of the nucleus by gemmules, these leading to the formation of male gametocytes. They were able to recognize a primary and a secondary cytoplasmic and a primary and a secondary intranuclear stage.

The relation of these parasites to the skin lesions is so definite and intimate as to lead to the conclusion they are the cause of the disease. The earliest lesions occurred in the corium antedating the epithelial changes. The endothelial cells of the dilated blood and lymph capillaries are swollen, often desquamating and sometimes proliferating. Mononuclear leucocytes begin to accumulate around the vessel. Bodies identified as gemmules may be seen in the blood and lymph vessels, and between them and the skin. There is hemorrhage by diapedesis and by rhexis into the tissues. Thrombosis, due to agglutination of red cells, could be seen. No endotheliolysis was demonstrable. No parasites within the endothelial cells were demonstrable. Now the papular stage is reached and the gemmules can be stained within the epithelial cells. The organisms lie in vacuoles within the protoplasm. The invaded cells become enlarged to several times the normal size. The nucleus shows no changes until the cell begins to break down, when it undergoes necrotic phenomena.

As the end of the primary cytoplasmic stage is reached

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(1) Journal Med. Research, October, 1904.
(2) Practical Medicine Series, 1904, Vol. IX.

fluid accumulates in the tissue. The secondary cytoplasmic stage begins in the deeper layers of the epidermis. The beginning of the primary intranuclear stage overlaps the secondary cytoplasmic. Some of the organisms undergo partial development without reaching the nuclei, and others that have grown into the nuclei burst the nuclear bounds and can be seen free between the cells. The secondary intranuclear stage is almost limited to the deeper epithelial cells. Seldom are any organisms found without the nucleus, but nearly every nucleus of the deeper layers contains them. The progress of the lesions is now at an end. There is much cell detritus present and many leucocytes gather in the lesions. At the margin of the lesion autoinfection with the development of a new cycle is prone to occur.

Comparative Histology of Vaccinia and Variola. Ewing,[1] having in mind the elaborate work on cells and cell changes in degenerations by Hückel,[2] v. Wasielewski,[3] Foa,[4] Sikorsky,[5] Albrecht[6] and Hertwig,[7] and the researches and conclusions of the Councilman school,[8] has studied vaccine material from the corneas of lower animals; material from variola lesions in man; tissues inoculated with diphtheria toxin, and skin lesions in frogs, and other animals of that group. A great many of the bodies within the protoplasm of cells he has been able to definitely connect with degenerative processes. Especially is this true of the degenerative processes which follow inoculation with strong diphtheria toxin. In fact, Ewing thinks there is much reason for believing the lesions of smallpox are due to some diffusible poison, such as diphtheria toxin. That not all of the stages described by Calkins, Councilman et al. have been found, Ewing thinks not strange since there is no other disease of which he knows, in which there is the same epithelial degeneration in combination with ef-

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(1) Journal Med. Research, November, 1904.
(2) Ziegler's Beiträge, II Sup. Hft., 1898.
(3) V. Wasielewski, Zeutbl. f. Bak., 1897, S. 901 and Zeitschr. f. Hygiene, 1901, S. 212.
(4) Archives de Parasitologie, 1904, p. 508.
(5) Archives des Sc. Biol., 1903, p. 461.
(6) Beiträge z. Path. Anat., 1903.
(7) Festschr. f. Hæckel, 1904.
(8) Practical Medicine Series, 1904, Vol. IX.

fusion of a fluid subsequently retained under pressure in contact with epithelial cells. He found no evidence that so-called parasitic bodies have any ameboid movement or show any proliferative changes.

As to the intranuclear bodies he is practically of the same opinion. There are many bodies which can be definitely shown to be derived from linin globules, which substance is normal to the nucleus. Others are identical with the degeneration bodies within nuclei, as described by Hertwig.

But there remain others which Ewing has never seen in any disease except variola. These intranuclear bodies and certain protoplasmic bodies he thinks specific for variola. He is not certain whether they are specific effects or specific causes.

The observations of Albrecht show that the nucleus has not a definite resisting membrane and therefore displacement of the nucleus, or a portion of it, and changes in the nucleus itself are much less significant than was once thought.

All in all, Ewing leans decidedly to the opinion that these bodies are not etiologic factors in variola or vaccinia.

In a later communication he goes much farther in his opposition to the views of Councilman on *Cytoryctes variolæ.* In a study entitled "The Structure of Vaccine Bodies in Isolated Cells"[1] he says that he does not accept the vaccine bodies as protozoan parasites, though he thinks them peculiar to vaccinia. He suggests the possibility that the etiologic factor of vaccinia may be located in these bodies, being perhaps an ultra microscopic parasite, or one whose protoplasm is closely tied to the protoplasm of the cell. Or there may even be so close a fusion of the cell protoplasm and the infecting parasite as to form a new substance—a mycoplasm—as is claimed by Erikssen and Tischler, by Detray and by Toumey for certain vegetable diseases. Or maybe a different technic may show a bacterium within the bodies. He made delicate adhesion preparations by lightly touching very clean slides to vaccinal

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(1) Journal Medical Research, February, 1905.

lesions, preferably on the cornea. Fifteen to twenty such preparations would empty a corneal ulcer. These slides were dried in the air, fixed with alcohol and stained with Nocht's stain. The bodies were always found perinuclear. Primarily they were red—staining with open reticular chromatic filaments. Ewing was certain these were areas of cell cytoplasm, into which some nuclear proteid had flowed. Definite connection both with the nucleus and with the cell reticulum could be demonstrated. The compact effect and the encapsulation, characteristics noted by other observers, Ewing interprets as artefacts. The body presently becomes blue—staining (basophilic) and next is converted into a mucin appearing and staining mass. Certainly in his opinion the open reticular appearance of the bodies when prepared in this way and their chemical reactions, each so different from the observations of Mallory, demand an entire reopening of the question of the etiologic relations of vaccine bodies to vaccinia. This necessity is not lessened by the probable specificity of the bodies since they may be specific degeneration products.

Histology of the Skin in Variola. To the question of the etiology of variola, Ferguson's[1] only contribution is the description of a small body seen in the hemorrhagic variety. This body is present in great numbers. They are of variable size, the smallest being the size of a coccus; others are much larger. They stain deeply and solidly with nuclear stains. Early in the lesion they are seen in the blood vessels; then they wander (apparently ameboid) into the deeper layers of the epidermis, and finally reach the vesicles and scabs. They are found both between the epithelial cells and in the protoplasm thereof. The primary microscopic lesion of smallpox is a dilatation of the lymph spaces of the corium. These extend to the prickle layer of the epidermis. The prickle processes are lost. The cells balloon. Other cells become compressed into reticulating bands. Liquefaction occurs. There is proliferation and some ballooning of the cells over and by the side of the central zone, so that to the touch we have a shot-like papule—in reality, we have a papule with a microscopic

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(1) Journal of Pathology and Bacteriology, November, 1904.

vesicle. The vesicle comes toward the surface, destroying cells before it. Now a cornification begins to extend from the margin of the papule down into the prickle cell layer underneath the vesicle. Finally there is a complete cornified layer extending from the corneous layer peripherally to the elidin layer, to the prickle cell layer under the vesicle—the vesicle is essentially outside of the skin and absorption and constitutional effects are at an end—restitution proceeds rapidly. Should secondary infection occur, however, the sequence is destroyed.

Just as the leucocytosis of variola is a lymphocytosis, so Ferguson finds the leucocyte accumulation within the tissue and within the vesicles is of the lymphocyte type. In fact, within non-infected vesicles he has never found that polynuclear leucocytes constituted 50 per cent of the white cells present.

He summarizes the early changes by saying that the intercellular lymph spaces are widened from the corium up into the malpighian layer, involving the loss by rupture of prickle processes. Some of the cells are elongated and compressed. Others rupture from cellular edema. The essential leucocytic accumulation is lymphocytic in type. The essential healing process is an extension of cornification under and around the vesicle.

Cultivation of Ameba. Musgrave and Clegg[1] describe the following method for growing ameba: Place 100 to 500 c.c. of aqueous fluid containing ameba in a sterile flask and to each 100 c.c. add .5 to 1 c.c. of broth of 1 per cent normal alkalinity and set aside for one to three days. Ameba will collect at the top. Thence transfer with a loop to agar plates. Enough bacteria to nourish them will be transferred with the ameba. The possibility of success is closely connected with the bacteria transferred. In six to forty-eight hours growing ameba can be seen with a low power. The best agar for stock is: Agar, 20; Na. Cl., 0.3 to 0.5; extract of beef, 0.3 to 0.5 to the litre with 1 per cent normal alkalinity to phenolphthalein. An excellent plan is to plate out some bacteria from the stools to be examined, and then to plant the ameba in the midst of a

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(1) Journal Infectious Diseases, March, 1905.

pure culture. If transfers of the growing ameba are not made promptly they are liable to die. Amebas will not grow in bacteria-free fluids, except in the pus from a liver abscess. In this instance it is supposed that the bacteria subsist on enzymes, but efforts to artificially reproduce liver pus fiuid as a culture media have failed.

The ameba from the human intestine are quite selective as regards the bacteria with which or on which they will grow. This selective action can be decreased or increased by varying the environment through a few generations. The best temperature is 68° to 82° F. They grow best at room temperature and poorly in the incubator. X-rays affect them unfavorably; sunlight inhibits and fluorescence causes encystment and death. Quinin kills them in solution of 1:2,500; acids kill them promptly.

Musgrave and Clegg are of the opinion that ameba are pathogenic. As to the controversy as to non-pathogenic and pathogenic ameba they are of the opinian that the size and shape of the protozoan have nothing to do with pathogenesis, nor can they be made a basis of classification. Finally they say that while all the evidence now at hand does not warrant us in concluding that all amebas are pathogenic, still all the known facts about this infection are compatible with this theory.

Amebas Affecting the Human Intestine With a Description of Two Species:—Entameba Coli and E. Dysentaria. Craig,[1] stimulated by the researches of Schaudinn (loc cit), has re-investigated the subject of multiplicity of species of Ameba coli and his changed his opinions expressed in 1904.[2] He now believes that two species are to be found in the human colon, Entameba coli and E. dysentaria.

Schaudinn[3] found Ameba coli in thirty-four out of sixty-eight inhabitants of East Prussia examined by him. Twenty-five per cent of the residents of Berlin examined by him and 256 of 385 residents of Austria examined showed this protozoan. He describes two species of parasite. Entameba coli and E. histolytica. Entameba coli divides as

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(1) American Medicine, May 27, 1905.
(2) Practical Medicine Series, 1904, Vol. IX.
(3) Arbeiten aus dem Kaiserlich. Gesundheit, 1903, Heft 3.

follows: I. Stage of reconstitution: (a) Division of the nucleus into two, each going to a pole of the ameba; (b) each of these nuclei divide and subdivide until there are four nuclei in each pole of the cell. Three of these are transformed into "brilliant" bodies; one persists as a nucleus. II. Stage of copulation. These two nuclei come back to the center. They divide and subdivide to make four. These arrange themselves into pairs so that one member of each pair comes from one of the first nuclei and one comes from the other. Each member of each pair now fuses with the other member of that pair. Now the two nuclei which remain divide and subdivide into eight daughter nuclei and each of these becomes encysted, so that the ameba contains eight daughter cysts.

According to Schaudinn, Ameba histolytica is characterized by the following points: Differentiation of the protoplasm into ecto- and endoplasm, slightly elongated nucleus and its location at the periphery of the endoplasm; poverty of the nucleus in chromatin; formation of small cysts at the surface and entire absence of encysted ameba showing eight daughter cysts.

La Sage[1] made use of cultures to differentiate the varieties of ameba. He succeeded in growing ameba seven times in thirty attempts. He selected small bits of mucus containing live, active ameba and placed them on agar on which there was a poor bacterial growth. Paracolon supplied the most advantageous growth. Another method was to place a piece of mucus on the side of a test tube in the bottom of which was a little sterilized water. The mucus dried slowly; the ameba became encysted, and these encysted organisms were used for culture purposes.

To rid ameba of intestinal bacteria he proceeded as follows: A vertical agar surface was selected. At the bottom the ameba were placed; at the top the nourishing bacilli were placed. In a few days the ameba had grown up and into the top culture. Then a loopful was taken from the top and the process was repeated on a new surface. After a few transfers all of the intestinal bacteria had been left behind. A study of these young ameba

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(1) Annales de l'Instit Pasteur, January, 1904.

showed the characteristics of hemolytica and never those of coli. The apparent secondary cysts seen were small surface extrusions. These small cysts were 3 to 6 *m.* in diameter. They contain some chromatin which has come from the mother nucleus and which later forms a nucleus. He used Laveran's and Marino's stains.

He concludes that Ameba histolytica is pathogenic; that A. coli is not, and that there are cultural and morphologic peculiarities by which they can be differentiated.

Stiles[1] has made a study of *Piroplasma hominis.* He believes the so-called bodies are in reality hemoglobin-free areas in the red corpuscles. Nor can he accept the proof as to the intermediate hosts.

Craig[2] comes to the same conclusions as Stiles.

An Epidemic of Trypanosomiasis Among White Rats. Terry[3] reports an epidemic of trypanosomiasis among the white rats of Rush laboratory. The animals had been used for some starvation experiments, and just after this some ordinary gray rats were introduced into the same laboratory and were kept in adjacent cages. In fact, a few of the gray rats escaped and were seen not infrequently with the white ones. Soon an epidemic of gangrene of the nose and toes was noticed amongst the white rats. Examination of the blood of all of the affected white rats showed trypanosoma in 90 per cent. Five weeks later, when there was no gangrene amongst the rats, seventy-six additional animals were examined. Of these apparently normal rats 37 per cent were found infected.

Two factors were held responsible for the decrease in percentage. In the first place rats tend to spontaneous recovery from trypanosomiasis. Some rats that had lost one or more toes from gangrene were found free from parasites. In the second place about one-fifth of the rats were born during the intervening five weeks and not one of these was found infected even though the mother had been infected while carrying these young ones. Fifty-four white rats from a different source showed about 7 per cent infected.

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(1) Marine Hospital and Public Health Service Bulletin, No. 20.
(2) American Medicine, Dec. 10, 1904.
(3) Transactions Chicago Pathological Society, April, 1905.

Sixty-four per cent of the wild gray rats around the laboratory were found to be infected.

Trypanosoma of Birds. Novy and Macneal[1] say that trypanosoma infection of birds is very common and widespread. Different species may harbor different species of trypanosoma, and one bird may harbor several species. Trypanosoma may or may not be associated with intracellular parasites and no constancy can be shown to exist between a given trypanosoma and a given cytozoon. The unsuspected frequency of trypanosoma infection in birds suggests that man may also be a host more frequently than is thought.

Ankylostoma Infection and the Presence of the Larva in the Skin. Goldman[2] tells the results of the warfare against Ankylostoma in Breunberg, where the morbidity from this disease among the miners has been reduced from 90 to 15 per cent.

Looss, of Cairo, at the First International Ankylostoma Conference (held at Cologne, August, 1904), showed specimens of the larva in the skin. Goldman remarks that many of his patients complained of eczemas and furuncles.

Looss produced infection in puppies by rubbing the larva on the skin. He was able to trace the path of the larva along the hair, through the lymphatics to the regional glands, and finally through the blood and lymph to the intestinal canal, where they mature.

Schaudinn, in Berlin, using the same method, has been able to infect apes, and to recover the adult parasite from the intestine, which viscus previously had been free.

Anemia in Porto Rico. Ashford, King and Ingaravidez[3] found 5,490 cases of uncinaria in a study made at Bayamen. In their opinion 90 per cent of the population of Porto Rica is infected. Of 951 cases of anemia, 947 were due to uncinaria. Of this 5,490 cases, 113 died, or were not improved by the treatment; 50 per cent were cured. Infection probably occurred more frequently through sores on the feet—ground itch, dew poison, etc.—than otherwise.

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(1) Journal Infectious Diseases, March, 1905.
(2) Wiener med. Woch., 1905, No. 2.
(3) Porto Rican Reports, December, 1904.

Wet dirt seemed to be necessary. The hemoglobin was sometimes as low as 10 per cent; 20 to 30 per cent was not infrequent; 40 to 70 very frequent. The number of red cells was sometimes 1,000,000 to 1,250,000, but 2,000,000 to 3,000,000 was the rule. The color index was low, indicating that the anemia was of the secondary type. The microcytic type of red cells was of the same significance. There was occasionally a general leucocytosis, though it was not the rule. In some cases 20,000 was reached. More cases gave a normal leucocytic count, and many showed hypoleucocytosis. A slight leucocytosis, 8,000 to 9,000, might be termed the rule. Eosinophilia was always present.

The great prevalence of this disease in tropical countries was well shown by the U. S. Commission in Porto Rico. That it is of great economic importance in temperate climates also is shown by the fact that 90 per cent of the workmen in the Rennberg district were affected.

Mode of Infection in Uncinariasis. Smith[1] reports observations that leave no escape from the opinion that this parasite can infect through the skin. He is not able to say that the skin is the only route of infection. The skin eruption tends to subside, to heal spontaneously in a few days, if it is not scratched.

The author exhibited a specimen, showing the stomach of the parasite containing cells from the intestinal mucosa of the host, and he calls attention to the fact first shown by Sangalli, that the parasite subsists less on the blood and more on the cells of the mucous membrane of the intestine.

Filaria in the U. S. Andrade[2] reports a case of Filaria sanguinis hominis in a man who had always lived in South Carolina and Florida. There was chyluria. Larval forms were found in the urine and in blood during the evening hours.

Filaria Loa. Wurtz and Clerc[3] report an infection of the skin and connective tissues of the hand with this parasite. There was a leucocytosis of 19,600, of which 53 per cent were eosinophiles. The worm was removed, but the

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(1) Journal American Med. Assn., Oct. 14, 1905.
(2) Amer. Jour. Med. Sci., July, 1905.
(3) Archives de Med. Experimentale et d'Anat. Path., March, 1905.

eosinophilia persisted. The authors do not say that these might not have been infections with other worms, or even with the same parasite, in a quieter form in some other locality.

The Parasite Theory of Carcinoma. E. von Leyden[1] says there has always been a rather vague feeling that carcinoma was an infectious disease. It was so considered by Sydenham and Van Swieten. Trauma, to which Von Hanseman ascribes much importance, is considered by v. Leyden as an exciting factor only; *e. g.*, a parasite may become more active after trauma. He says carcinoma must be considered as a local disease. Most carcinomas occur in localities which are very readily infected (mouth, digestive tract, internal and external genitalia). Carcinoma occurs in all animals. It has been reported even in fishes and amphibia. Geographically it is more abundant in temperate zones than at the equator or colder zones. As an additional argument for the infectiousness of carcinoma, there is a fairly abundant literature on carcinoma, in both man and wife (*carcinome a deux*). There is mention of epidemics of carcinoma. Like tuberculosis, it is not inherited, though there may be an inherited predisposition. Cases are recorded in which carcinoma of the lower lip was followed by carcinoma of the upper, and carcinoma of the left side of the vagina inoculated the right wall.

Hanau caught a wild rat exhibiting a carcinomatous growth. Pieces of the tumor were inoculated in another rat with success. The tumor was reproduced in the second rat.

Orth[2] says that no one up to the present time has produced proof that carcinoma is of parasitic origin, and that there is no necessity for assuming a parasitic etiology. Every carcinoma is composed of epithelial cells which have grown from pre-existing epithelial cells, and which retain for a long time the characteristics of the cells from which they have sprung. For example, if we examine a metastatic carcinoma of the liver, we find the

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(1) Berlin klin. Woch., 1905, No. 13.
(2) Annals of Surgery, December, 1904.

liver stroma and the liver epithelial cells either quiet or undergoing retrograde changes. It is the imported cell which is doing all of the things peculiar to carcinoma. He says: "I do not consider it impossible that an intracellular parasite is playing a part, but it is impossible for it to play a part independent of the epithelial cell. It cannot possibly in itself be the decisive factor in the new growth."

Von Hanseman[1] argued against the parasitic theory. He said that inoculation experiments were not of much value so long as both epithelial cells and the socalled "parasites" were placed in abnormal locations by inoculations.

L. Michaelis has successfully inoculated rats subcutaneously with fluids pressed out of carcinomata. The inoculation in rats was positive, even in the fifth generation.

It has been suggested that the carcinoma micro-organisms are inoculated into the skin by insects, like malaria. v. Leyden is somewhat skeptical about this.

As far as the histology of carcinoma is concerned, cellular inclusions are probably responsible for the disease. Cellular inclusions in carcinomatous cells have been noticed by Virchow and others. The former took them for vacuoles, or products of cellular degeneration, decay. Others have taken them for leucocytes, lymphocytes, degenerated nuclei. v. Leyden considers them as being of parasitic origin, or parasites, and compares them to the eyes of birds. He does not accept Micrococcus neoformans and the other bacteria, claimed to be etiologic agents.

The chemistry of carcinoma fluids differs from that of the ordinary cells of the body. Blumenthal was able to obtain from the carcinoma tissue a ferment which had an autolytic action upon the normal cells of the body. (See also Buxton Journal Med. Research, 1904-05.)

An Immune Body Inhibiting the Development of Cancer in Mice. Clowes[2] used some white mice infected with adeno-carcinoma which Gaylord had obtained from Jensen in 1904. These tumors were inoculated into other mice, grey and white. It was noted that a considerable number of mice, in which a carcinoma had grown to some size,

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(1) Journal American Med. Assn., April 15, 1905.
(2) Johns Hopkins Hospital Bulletin, April, 1905.

would begin to improve, the tumor would disappear and the animal would return to health. Mice in which there were carcinomas were then treated with serum from animals that had recovered. The experiments were controlled in each instance by mice with tumors of the same ages and sizes. All tumors of less than 3 to 4 grains in weight promptly disappeared. Two c.c. was the dose usually employed and cure was generally effected in a few days. The carcinomas in the treated cases showed simple atrophy of the epithelial cells, and hyperplasia of the connective tissue elements. The serum from the mice which had been cured

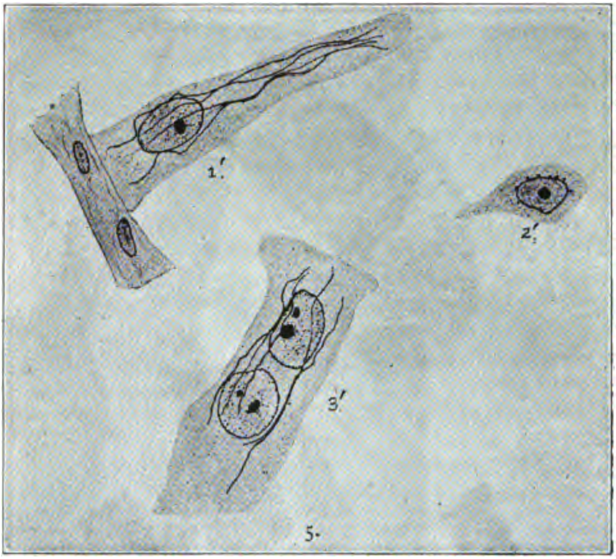

Fig. 7. Intracellular Fibrils.

Camera lucida drawing. Zeiss 2 mm. objective. No. 2 ocular.

1'. Shows the spreading of the fibrils about the nucleus and the gradual fading and disappearance into the cell protoplasm.

2'. Cross section of a cell, shows contact of fibrils with the nucleus.

3'. Shows relation of fibrils to two nuclei in a single cell (compare with Fig. 4).

by serum did not seem as potent as that from mice spontaneously cured. The serum from mice cured with x-rays did not seem to have curative power. The immunizing substance did not act like a cytolytic body. It was not hemolytic. It was not curative for the tumors of large size.

Intra Cellular Fibrils in a Malignant Tumor of Epithelial Origin. Wolbach[1] reports a malignant villous papilloma, originating in the bladder, which had penetrated the wall and invaded the pubic bone. The bone was soft and cancellous, and a yellowish puriform fluid could be expressed. The tissue was removed two hours after death, and placed at once in Zenker's fluid. It was stained with Mallory's phosphotungetic acid-hemotoxylin. It showed abundant wavy fibrils within the epithelial cells, running frequently into contact with the nucleus, but never through it. The fibrils were not found in mitotic epithelial cells and no relation to mitosis was demonstrable. They seemed connected with the cell reticulum. They were found in no cells except those of the carcinoma areas (Fig. 7).

The Nature of Cell Inclusions of Cancer. Greenough[2] reports the results of his further study of tissue, with relation to Plimmer's bodies. He has searched for these bodies in 177 tissues, and found them in 94. He tabulates his work with that of Nösskie, Nichols and Honda, and the result is a report on 481 specimens. Plimmer's bodies

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(1) Journal of Medical Research, May, 1905.
(2) Journal Medical Research, January, 1905.

Figs. 6 and 7. Adeno-carcinoma of the breast. Arrangement of cells around a gland lumen, and inclusions in the cell protoplasm on the lumen side of the nucleus. Specimen No. 9.

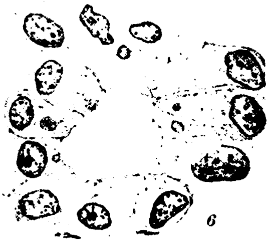
Fig. 8. Adeno-carcinoma of breast. Arrangement of cells around a gland lumen, and inclusions on lumen side of nucleus. Specimen No. 26.

Fig. 9. Cyst-adenoma of breast. Gland acinus with proliferated epithelium, and inclusions on lumen side of nucleus. Specimen No. 33.

Fig. 10. Adeno-carcinoma of breast. Arrangement of cells around a gland lumen, and vacuolar inclusions without central body in that portion of the cell toward the lumen of the duct. Specimen No. 28.

Figs. 11 and 12. Adeno-fibroma of breast. Two gland tubules, with inclusions on lumen side of nucleus, and evidence of secretion vacuoles in the open lumen of the duct. Note variation in size and in staining of central body of inclusions. Specimen No. 60.

Fig. 13. Chronic cystic mastitis. Gland acinus with proliferated epithelium. Inclusions in cell protoplasm toward the lumen of the duct. Specimen No. 38.



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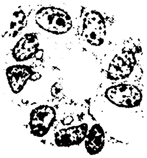

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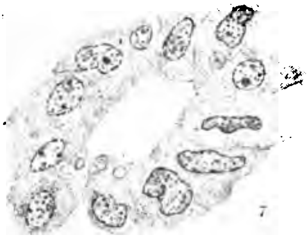

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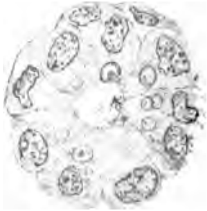

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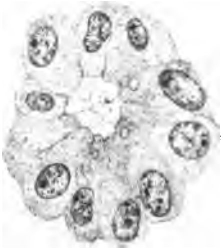

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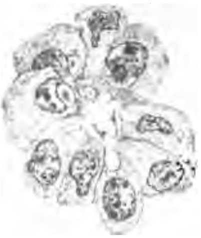

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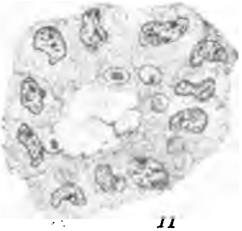

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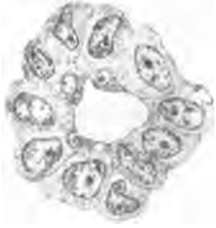

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were found in 217. Analysis of the tables shows: Glandular carcinoma, 185 cases, 83 per cent positive; sarcoma, 30 cases, 3 1-3 per cent positive; suprarenal tumors, 5 cases, 80 per cent positive; epithelioma, 79 cases, 0. per cent positive; adenoma, 15 cases, 13 per cent positive; non-cancerous disease of breast, 72 cases, 68 per cent positive; miscellaneous, composed principally of normal tissue and of the infectious granulomata, 95 cases, of which 7 per cent were positive. He is of the opinion that the bodies are vacuoles, the result of cell secretion, and that the central, or so-called "nuclear material," is, in reality, coagulated albuminous substance which has shrunk away from the cell periphery.

The Mixed Tumors of the Lacrymal and Salivary Glands. Verhöff[1] disagrees with Warthin,[2] Veasey[3] and M. Frank[4] as to the nature of these much discussed tumors. In the parotid and lacrymal glands one occasionally finds a tumor presenting cells and a cellular arrangement such as can be interpreted as adenoma, or endothelioma. In addition there is usually a good deal of irregularity in the connective tissue development. There may be cartilage, or, on the other hand, there may be such immaturity as to suggest sarcoma. The tumor is usually encapsulated. It is generally outside of the gland capsule. Its capsule may or may not be connected with that of the gland. They vary in malignancy, as do all malignant tumors, but, speaking generally, they can be termed "semi-malignant."

He gives a detailed study of one tumor of the cylindroma type of the lacrymal gland. In addition he found 4 other specimens which had been preserved in the laboratory for years. These he examined as thoroughly as the circumstances allowed. Two of these were of the cylindroma type. One was sarcoma and one myxochondroma. Verhöff thought all of them adenomas, for the following reasons: (1) Their close connection with the lacrymal gland; (2) the presence of gland-like lumina; (3) the lining cells showed a fenestrated internal membrane with double dots in the centers of their distal end; (4) the presence of a basement membrane of connective tissue; (5) the occurrence of cell masses, containing pearls, keratohyaline granules and prickle cells, and (6) the occasional presence of spiral fibres between the cells of the parenchyma. By fixing the specimens in Zenker's fluid and staining with Mallory's phosphotungetic acid-hemotoxylin, Verhöff found a delicate fenestrated membrane at the inner side of the epithelial cells of the glands. In the centers of the fenestrations were two dots, which are probably centrosomes. This membrane he has never found in any other than epithelial structures.

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(1) Jour. Med. Research, February, 1905.
(2) Archives of Ophthalmology, 1901, p. 601.
(3) Medicine, November, 1902.
(4) Medical Record, Jan. 9, 1904.

By the same method he demonstrated fibrils between the cells. These he thinks are also characteristic of epithelial structures (Figs. 6 to 13).

Fatty Degeneration. Christian[6] studied the pathology of Fatty Degeneration. He believes that the fat granules and globules found in the cells during fatty degeneration are not derived from the proteid of the cells. In the main, the fat is transported to the cells from fat depots elsewhere. He thinks some of it may come from fat related bodies within the cells, though not from proteids. He says that of fatty degeneration in the sense used by Virchow we have no proof. He thinks that the question will be solved finally by the use of improved technic. The objection to the use of osmic acid is that it does not stain all fats, but only olein and oleic acid. He prefers Scarlach R. and Sudan iii. Of these he uses the former more frequently, because it stains fat more and other tissues less intensely than Sudan iii, and it is less liable to precipitate in the tissues. He stains with a saturated solution in 70 per cent alcohol for 24 to 48 hours, or in a saturated alkaline-alcoholic solution, as suggested by Herxheimer. He used sections made by freezing, and mounted in glycerin.

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(1) Verhoeff, Royal London Ophthalmic Hospital Reports, 1903.
(2) Lewy-Virchow's Archiv, 1903, 236.
(3) Mallory Journal Medical Research, 1903, 334.
(4) Herxheimer Arch. f. Derm. u. Syph., 1889, 645.
(5) Eddowes, Montschefte f. prak. Dermat., 1890, X, 89.
(6) Johns Hopkins Hospital Bulletin, January, 1905.

SPECIAL PATHOLOGY.

Diseases of the Blood and Ductless Glands. Pernicious Anemia. Gulland and Goodall,[1] as the result of minute study in 17 cases of pernicious anemia, conclude as follows: (1) The essential feature of the disease is a megaloblastic anemia. (2) The evidences of destruction of blood in *so many* organs of the body argues against any actively destructive agent in these organs. It argues for such a vulnerability of the red cells as makes it possible for them to be destroyed in the liver, spleen or almost any organ. (3) The accumulation of iron in the liver is not peculiar ,to pernicious anemia. Some of it is due to destruction of red cells by endothelial cells and leucocytes within the liver, but most of it is due to destruction outside of the liver, the katabolic iron being transported to the liver and there deposited. (4) The intestines are not the site of special or specific changes. The toxin (which, acting on the bone marrow, causes a megaloblastic rather than normoblastic type of blood regeneration) may be produced in the intestine, or it may be produced elsewhere. (5) The megalocytes and megaloblasts fall a ready prey to endothelial cells and leucocytes in the hemolymph glands, spleen and marrow.

The authors do not note the presence of any nervous phenomena in their short clinical reports, nor do they report any examinations of the nerve structures. While these phenomena are of great interest, from the standpoint of the clinician, at the same time they are secondary phenomena and their study concerns itself largely with what may be regarded as the etiologic phenomena. They consider the blood largely from the standpoint of whether it is megaloblastic or normoblastic, though they make no note of having measured the corpuscles on a set plan, such as is offered by the volume index of Capps.

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(1) Journal Path. and Bacteriology, January, 1905.

The essential points in their opinion are: Is the blood of a megaloblastic type, and, are the marrow changes of the megaloblastic type? Focal necrosis in the liver, giant cells there, excess of liver iron, enlarged hemolymph glands —all these are of secondary importance. Giant cells in the liver, similar to megaloblasts, they suggest may mean that the liver. is returning to its fetal labor as a blood maker. Interesting is their observation that the primary factor is a toxemia and that the toxemia is paroxysmal, owing to temporary relative immunity. Thus they account for the periodicity of pernicious anemia.

Etiology and Pathogenesis of Pernicious Anemia Bunting[1] is in accord with the conclusions of Gulland and Goodall. In fact, he brings to them some evidence adduced from experimentation. Repeated bleeding of rabbits produced an anemia of the secondary anemia type. The nucleated red cells were of the normoblastic type. Sixteen normoblasts were counted in counting 500 leucocytes. The bone marrow showed an increase in normoblasts. Other experiments consisted in injecting rabbits with myelotoxic and hemolytic sera. Here the anemia was of the pernicious anemia type. The number of nucleated red cells showed such figures as 1,130 normoblasts, 603 naked pyknotic red cell nuclei, and 335 megaloblasts per c.m. in one case, and 3,472 normoblasts, 2,884 naked nuclei, and 400 megaloblasts per c.m. in another case. Further experimentation was done with ricin, a soluble toxalbumin, derived from the castor bean. This drug produces numerical reduction of red blood corpuscles, hemoglobinuria and pigmentation of the spleen and lymph glands. Rabbits injected with ricin showed the same pernicious anemia type of lesions as those injected with myelotoxic and other hemolytic sera. The bone marrow changes were of the pernicious anemia type. There are two hematogenetic groups in the marrow—the leucoblastic producing leucocytes and the erythrogenetic producing red blood corpuscles. In the centre of an erythrogenetic group are large nucleated hemaglobin containing cells—megaloblasts. These divide and so the maturing cells are pushed peripherally. Peripheral

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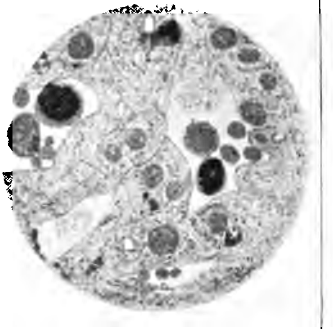
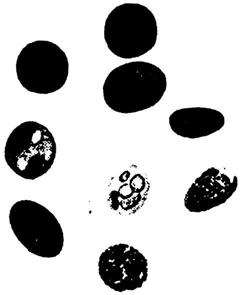
(1) Johns Hopkins Hosp. Bulletin, June, 1905.





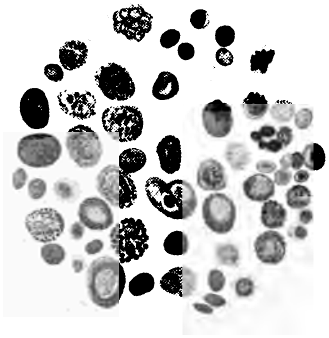


Fig 4

to these are nucleated red cells, with vesicular nuclei; outside of these normoblasts with pyknotic nuclei and peripheral to these normal red blood corpuscles. Now, in secondary anemias the demand for new cells rushes normoblasts, occasionally vesicular nucleated red cells, and very rarely, megaloblasts into the blood stream. In the pernicious type the marrow usually shows marked changes in the megaloblastic, central zones, and large numbers of these embryonal, very immature cells are thrown into the circulation. In the anemias from the toxemias which were artificially produced, the megaloblastic areas of the bone marrow were especially involved. Bunting's investigations support many of the old theories of Hunter. Like Hunter, he thinks the toxin is probably produced in the intestinal tract, but he differs from Hunter in thinking the action is exerted on the bone marrow, rather than that it is a hemolysis located in or near the portal area. The cord lesions, the gastric atrophies, etc., he thinks are secondary and their existence argues for a toxemia. For example, the severest forms of secondary anemia never produce cord lesions—many toxemias do so. He cites the observations of Minnich (Zeitschrft. f. kl. Med., Vol. XXI., p. 310), that ergotism, pellagra and lathyrismus produce similar lesions. He is in accord with Bloch (Folia Hemotologica, 1904, Vol. I, p. 271), that pernicious anemia

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Fig. 1. From submucosa of intestine, showing basophils. Eosin, methylene-blue. (×1000.)

Fig. 2. Liver, showing giant cells and a phagocyte whose characters are altogether obscured by iron pigment. Pot. ferrocyanid, HCl, carmalum. (×1000.)

Fig. 3. A collection of giant cells and phagocytes from necrotic areas in the liver. Eosin, methylene-blue. (×1000.)

Fig. 4. Very thin section of bone marrow of Case 17, showing a phagocyte and a basophil with the large granules, and other characteristic cells. Eosin, methylene-blue. (×1000.)

Fig. 5. Photograph of submucosa of intestine, showing basophils with large granules. (×50.)

Fig. 6. Photograph of necrotic area in liver, showing giant cells. (×200.)

Fig. 7. Photograph of liver, showing iron reaction and great fatty change. (×200.)

Fig. 8. Photograph of a section of spleen, showing great accumulation of iron pigment. (×50.)

Fig. 9. Sketch of liver, showing stored iron at the periphery of a lobule and iron in endothelial cells towards its center. (×400.)

Fig. 10. Sketch of bone-marrow section, showing accumulation of iron pigment along the endothelium of a small vein. (×600.)

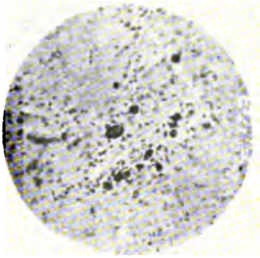


Fig. 5.

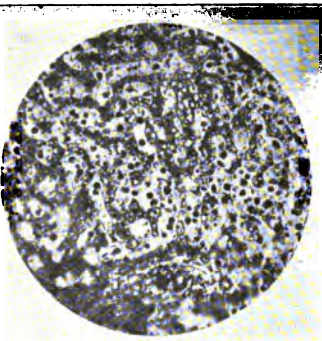
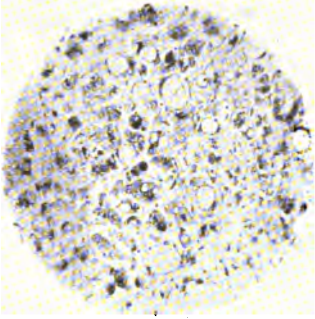


Fig. 6.



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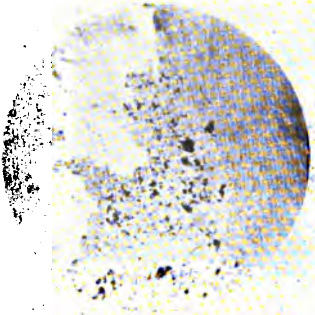

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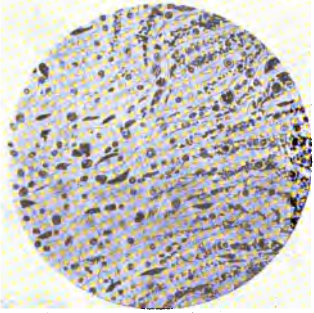

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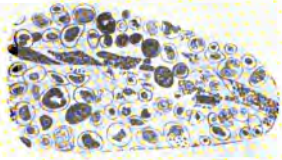

Fig. 10.

rests almost always on an asthenic condition of the hemoporetic system, and after citing a long list of frequently ascribed causes, he says they are either incidental associations or secondary effects.

Effects of Periodic Loss of Blood. Smith[1] was stimulated to investigate the blood from observing that horses used for the manufacture of antitoxin, in the course of time became delicate and frequently died from apparently insufficient causes. His investigations related to hemolysis. Having standardized his methods satisfactorily he proceeded to determine the strength of salt solution which caused hemolysis. 0.42 per cent caused hemolysis of 99 per cent of the red cells within 30 minutes; 0.60 per cent caused lysis of .5 of 1 per cent in 2 hours. He called this range the normal resistance range in the horse, following Hamburger in this (Osmot Druck in Iononlehre, 1902). The greatest destruction is at 0.48. Comparing the bloods of horses that had been frequently bled for antitoxin, he found a resistance range of .52 to .64. The greatest destruction was at .56 to .57. In other words, there was greater hemolysis, the blood went to pieces more easily in animals that had been repeatedly bled than in those that had not. But there are many factors that might be the cause of this. Might it not be due to the repeated injections of toxin, or to the presence of antitoxin. Smith's work argues against both of these factors. Nor does he think it likely that the difference was accidental and due to the peculiarities of the horse. Nor was it due to the peptone injected with the toxin. Experimentation showed that the osmotic tension of the serum does not adapt itself to changes in the corpuscles. There is not normally a close relation between osmotic tension of the serum and of the red blood cells. For example, whilst the red blood cells begin to lose hemoglobin at .58 to .60, the normal salt contents of serum is 0.9 to 0.95.

Smith thinks that the repeated bleeding alone can be charged with the lowered resistance of the red cells.

Aplastic Anemia Associated With Lymphoid Hyperplasia of the Bone-Marrow. Blumer[2] reports a case which,

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(1) Johns Hopkins Hospital Bulletin, 1905.
(2) Journal Med. Research, October, 1904.

from a clinical standpoint, presents all the leading characteristics of progressive pernicious anemia, yet neither the blood picture nor the pathologic findings correspond to those of ordinary pernicious anemia. In fact, the blood shows nothing in common with pernicious anemia, except its progressive character, and the leucopenia with the relative increase in the mononuclear leucocytes.

In the peripheral blood there was a progressive loss of red corpuscles without any marked variation in the size or shape of the cells and without nucleated reds. There was a diminution of number of leucocytes and relative increase in the mononuclear forms, with almost complete absence of cells with granular protoplasm. In places there was a hyperplasia of the mononuclear elements of the bone-marrow.

There are indications that the disease clinically termed "aplastic anemia" is not a pathologic entity, but may be due to a variety of causes. Three main groups of this disease may be recognized: (1) Cases in which the lesions are those of progressive pernicious anemia. (2) Those in which the bone-marrow shows primary aplasia. (3) Cases where there is a hyperplasia of the mononuclear elements of the bone-marrow. In this case hyperplasia showed only in places. The shafts of the long bones showed none.

Smears from the tibia showed blood having the same characteristics as peripheral blood. Smears from the vertebral marrow showed a marked hyperplasia of the lymphoid elements. An average examination of the peripheral blood showed as follows: Percentage hemoglobin, 20; number of red cells, 1,400,000; number of leucocytes, 4,000. An average of 3,200 leucocytes gave the following percentages: Small mononuclears, 90 per cent; large mononuclears, 2 per cent; polynuclears, 8 per cent. Smears from the vertebral marrow showed small mononuclears, 98.52 per cent; large mononuclears, 0.28 per cent; polynuclears, 0.03 per cent; polynuclear eosinophiles, 0.03 per cent; neutrophilic myelocytes, 0.18 per cent; basophilic myelocytes, 0.21 per cent; atypical forms, 0.75 per cent. Blumer thinks that Senator's case(1) and that of Wolf(2) were alike, but that they differ from that of Muir,[1] in that the marrow was lymphoid and hyperplastic throughout, rather than fatty.

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(1) Zeitsch. f. klin. Med., LIV, Hft. 1, 2.
(2) Berlin. klin. Wochenschr., 1901, No. 2.

Influence of Complicating Diseases Upon Leukemia To the subject of curability of leukemia Dock[2] contributes an article on the relations of intercurrent infections to the course of leukemia, and especially to the blood picture of the disease. He reports 3 cases. The first had a typical myelogenous leukemia with a leucocyte count as follows: Total number per c.m., 367,070; small lymphocytes, .0 per cent; large lymphocytes, 0.30 per cent; polymorphonuclear neutrophiles, 41.6 per cent; polymorphonuclear eosinophiles, 0.7 per cent; mononuclear eosinophiles, 1.4 per cent; myelocytes (Ehrlich), 48.8 per cent; basophiles, 2 per cent; degenerated leucocytes, 5 per cent. A month later she contracted influenza and her count was as follows: Total number of leucocytes, 5,000; small lymphocytes, 1.6 per cent; large lymphocytes, 13.3 per cent; transition forms, 3.3 per cent; polynuclear neutrophiles, 63.8 per cent; polynuclear eosinophiles, .3 per cent; mononuclear eosinophiles, .6 per cent; myelocytes, 9.6 per cent; basophiles, 1.0 per cent; degenerated forms, 6.6 per cent. About two weeks later the total count began to rise gradually and one year later it was back to the former figures.

Studying the effects of tuberculosis upon leukemia, Dock reports 2 cases, one a case of severe tuberculosis of serous membranes, associated with leukemia. In this case for two years, while under Dock's observation, there was no effect on the blood cells. A year later, the patient having died from tuberculosis, no blood changes were to be found. The necropsy showed no evidence of leukemia, except lymphoid bone-marrow. In the next case, a man with leukemia developed a miliary tuberculosis of moderate extent. It did not seem to influence his leukemia.

Contribution to the Pathology of the Thymus Gland. It is the opinion of Dudgeon[3] that the usual necropsy rec-

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(1) British Med. Journal, 1900, II, p. 909.
(2) American Journal Medical Sci., April, 1904.
(3) Journal Pathology and Bact., January, 1905.

ord, relative to the condition of the thymus gland, is misleading. This gland never disappears at any time of life and failure to find it is due to hasty effort. While it loses no weight between the second year and puberty there is loss of Hassall's corpuscles—the epithelial element—and of lymph tissue, the weight being maintained by an overgrowth of fibrous tissue and an infiltration of fat. Two of his groups of pathologic thymuses are interesting. In marasmus the gland is atrophic. In many cases of sudden death the gland is hypertrophic. The reports of the average size of the normal gland vary greatly.

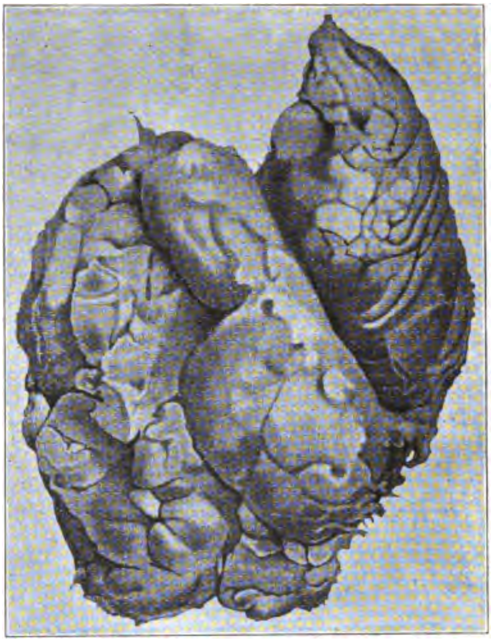

Fig. 11. Enlarged thymus gland. Case of sudden death in an infant. Wt. of glands, 34 grms. (Natural size.)

For instance, Jacobi says, 1 to 200 grains; Testut, 5 grains; Osler, Vierort and Friedleben give 25 to 30 grains;

Dudgeon thinks 7 to 10 grains is normal. He especially cautions observers not to mistake a certain process, which is physiologic, for abscess. When a thymus is left post-mortem for a few hours the center of each lobe is found to be occupied by some milky fluid. This fluid is filled with lymphocytes, which Astley Cooper compared to chyle. Dudgeon thinks it due to auto liquefaction. Tuberculosis and syphilis of the thymus he thinks exceedingly rare.

In marasmus, from any cause, there was atrophy of the thymus. Dudgeon divides his cases into two groups—primary atrophy, in which no cause of the marasmus could be found, unless it lay in the atrophic thymus, and secondary, in which there was other causes, such as generalized tuberculosis. In this last group the glands were quite as small as in the first, the minimum figures being 0.905 grains for the primary, and 0.345 for the secondary. The description does not indicate any histologic differences in the two types, except it be in degree. The fact of such similarity throws some doubt on the thymus as an etiologic factor. May it not be an effect in each? We know of no figures as to the relative decrease in the weights of the different organs in marasmus.

In a collection of 16 cases of sudden death in children under 12 years of age, the average weight of the thymus was found to be 25.11 grains. The largest weighed 47.05 grains. These enlarged glands showed the central lymph-juice collection on standing. Histologic examination showed nothing except a very large number of eosinophile cells of four types. These cells furnished about 20 to 50 per cent of all the cells of the gland and 95 per cent of the eosinophiles were large cells with a single oval nucleus, sometimes granular and sometimes not. This cell is not a blood cell. The other 5 per cent or less were the blood eosinophiles.

The relation between enlarged thymus and sudden death is obvious, yet the reason for it Dudgeon cannot ascribe. Perhaps he leans to the pressure theory of Jacobi. There is relation between rickets and enlarged thymus, between lymphatism and enlarged thymus, between Graves' disease, lymphatism and enlarged thymus, and in each of these there is tendency to sudden and usually unexplainable death.

Of interest also were Dudgeon's observations on the condition of the thymus in 33 children dying of acute diseases. Hemorrhages into the thymus were found in 55 per cent of the children dying from pneumonia.[1]

Tumors of the parathyroids microscopically were composed of tissue closely resembling that of a parathyroid. As compared with normal gland the blood supply was extremely meager. There were strands and branched masses of cells, separated by a delicate stroma, bearing blood vessels. The cells are arranged in columns and press one another into polygonal forms. The cells resemble those of normal glands. They show vesicular nuclei and protoplasm, which may be faintly granular or perfectly clear and free from granules which stain. Large and small groups of cells, corresponding to the normal oxyphilic cells of parathyroid, are scattered among the other cells. Their protoplasm has a ground glass appearance and takes a deep eosin stain. Their nuclei vary in size and stain deeper than other cells. Mitotic figures occur in all these cell forms.

In certain of the cells masses of a central cavity are found, about which the cells have a palisade arrangement. The oxyphylic, as well as the ordinary cells, may take part in forming the walls of these follicle-like cavities. The cavities contain a finely granular coagulum, or are filled with bubble-like vesicles about the size of red corpuscles.

In first two cases there were colloid droplets scattered among the cells, but in last no trace of colloid material was found. It can be seen that, except in the size of the cell masses, the bulk, and the formation of such definite cavities, these tumors do not differ from normal parathyroid, unless it be there is no adipose tissue between the cell strands.

The theory has been advanced that this is merely a compensatory hypertrophy, but the author thinks it to be an adenomatous new growth.

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(1) See Ruhrah, Stokes & Rohrer, Am. Jour. Med. Sci., 1902, CXXIV, p. 841.

ORGANS OF THORAX.

Blood in Lobar Pneumonia. Rosenow[1] examined the blood bacteriologically in 175 cases of pneumonia, finding the pneumococcus in 91 per cent. In 11 of the 15 negative cases only 1 examination of the blood was possible. In 80 cases smears of blood were made and stained for pneumococci. In 47 of these a positive result was obtained. It seemed that the number of bacteria in the blood diminished toward the crisis, though conclusions from the number of bacteria found must be quite guarded. In general he found the higher the leucocyte counts the fewer the number of colonies from a given quantity of blood. In cases with 35,000 to 43,000 leucocytes per c.c., each c.c. of blood showed 0 to 25 bacteria to the c.c. In cases of leucopenia the number of bacteria was 100 to 1,350 per c.c. of blood used. The agglutinating power of the blood was found to be determinable as early as the second day of the disease. It increased up to the crisis and decreased thereafter. It was never obtainable with a dilution greater than 1 to 50.

Normal blood serum is not bactericidal for pneumococci. They grow well on it; nor does it precipitate pneumococci. Pneumonic blood serum is also not bactericidal for pneumococci. They grow well on it, but in liquid pneumonic serum media, on which pneumococci is growing, a heavy precipitate appears, due to the formation of acids in excess.

Histogenesis of the Tubercle. James Miller.[2] The lesions due to the tubercle bacillus are peculiar and in the main specific. That they are so is dependent upon several biologic peculiarities of that organism. In so far as other bacteria or foreign bodies approach the conditions that prevail with tubercle bacillus do the lesions approach those of tubercle bacillus. It is a live entity, mild in character, slow growing and with a resistant envelope. Either alive or dead it differs from many other similar irritants, in that it contains a poison capable of leaving the bacillus, and causing death of cell protoplasm, in whole or in part, fol-

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(1) Jour. Amer. Med. Ass'n, March 18, 1905.
(2) Journal Path. and Bacteriology, November, 1904.

lowed by caseation of the necrotic area. The essence of the tuberculous process in the opinion of Miller is phagocytosis.

It is to be noted that his experiments were made in the livers of rabbits. The tubercle bacilli were injected into a mesenteric vein. This may explain the prominence of blood cell phenomena.

Six hours after the injection a coagulum was seen, composed of serofibrin—which did not stain with the usual fibrin stains—and granular and nongranular leucocytes. The leucocytes, which speedily accumulate around the mass, are both granular and nongranular. The polymorphonuclear neutrophiles are probably the first to arrive on the field. They are actively phagocytic, but they soon show phenomena of necrosis, and many of them are digested by the mononuclear forms. Neutrophilic granules are frequently found loose. This may be a biologic phenomena, making for the destruction of bacilli or their poisons, or it may be a step in cell necrosis. Eosinophilic cells are found in fair abundance a day or two after the inception of the process. These cells are actively phagocytic. A few leucocytes with basophilic granules appear. These are also phagocytic, but their relatively small number makes it improbable that they play any considerable rôle in the combat against the infection.

Practically simultaneously with the invasion by the polynuclear leucocytes there is invasion by the mononuclear hyaline forms. Many and possibly most of these were the preëxisting lymphocytes and large mononuclears of the blood stream. No one can say with certainty that the cells of this type are not made by the endothelial cells, and possibly by the connective cells in situ or even by the adventitia cells. Of greater interest, however, is the work of these cells. They are mobile and phagocytic. They do not engulf bacilli as promptly as do the granular leucocytes, but they seem to have greater power to destroy them, and, in fact, are frequently found destroying the granular forms. As soon as the cell takes up a bacillus one sees a vacuolated area, and then an area that is recognizable as necrotic and, at times, caseated. These cells grow in size, begin to show large vesicular nuclei and deep staining protoplasm. They are thus the epitheloid cells. They send out pseudopodia, which entwine with others to form the tubercular reticulum. Others fuse their protoplasm with neighboring epitheloid cells to form giant cells. The pseudopodia of giant cells are the pseudopodia of the constituent epitheloid cells. In giant cells there are always zones of necrosis, due to local bacterial action. The giant cells are actively phagocytic for bacilli and for various other cells. At the periphery of the growing tubercle one sees smaller, more deeply staining cells.

Close study of these has convinced Miller that these are mononuclear leucocytes on the way to form epitheloid cells. The local connective tissues undergo some mitotic division, and probably more amitotic division, yet it seems probable that these cells do not help very much in the development of the tubercle. Miller is certain that the mononuclear leucocytes develop into the fibrous tissues which form a part of the tubercle. The connective tissue cell has a very limited range of motion. The leucocyte, of course, is much freer. In fact, a mononuclear leucocyte, impregnated with tubercle toxin, may be swept away to a new area and start a new tuberculosis, even though the cell contain no bacilli. This, he thinks, is an explanation of the large number of lesions in miliary tuberculosis, in which no bacilli can be demonstrated. The angioblasts of a tuberculosis may produce a few new blood vessels, but the number is small. The tubercle is relatively an anemic zone. This, however, is not the largest factor in the necrosis and caseation. These phenomena are due principally to poison. The elastic fibres speedily disappear from a tuberculous area.

Frequency, location and mode of dissemination of Tuberculosis, with special reference to its occurrence in lymph nodes, and during childhood. Harbitz[1] made a careful search for tuberculous lesions in autopsies on 275 children. One hundred and seventeen, or 42.5 per cent, were found tuberculous, although in not all of them were the lesions demonstrable with the unaided eye. In 12, in which no microscopic lesion was found, the microscope and the re-

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(1) Journal Infectious Diseases, March, 1905.

sults of inoculation showed tuberculosis. **Harbitz** always found hyaline degeneration indicative of tuberculosis. Large cell hyperplasia he did not regard as very significant. Of the 117, 72 died of tuberculosis, 21 had latent tuberculous lesions and 18 had latent bacilli. Of the 123 autopsies on children under 1 year, 14 died of tuberculosis, 2 had latent lesions and 9 latent bacilli; total, 25.

In series II, 142 autopsies there were 91 without demonstrable lesions, and of these, 18 showed latent bacilli. Of these 18, 10 were under one year of age. The cervicals contained bacilli in 13 instances; the mesenterics in 3. He quotes Thue as having found the mesenteric nodes involved much more frequently. He thinks that the possibility that tubercle bacilli may lie dormant for years, cannot be denied, though it is not probable.

He quotes Volland[1] as saying that of 2,506 persons under 24 years of age, 94 per cent had some glandular enlargement. Harbitz does not think all of these enlargements are tuberculous. Oftentimes they are, but more often they are not. As to congenital tuberculosis he quotes Warthin and Corrie[2] as thinking that congenital tuberculosis is of greater importance than is generally supposed. He agrees with them. He found proof of location of the primary lesion, in his opinion, as follows: Respiratory tract, 41 per cent; digestive system, 22 per cent; respiratory or digestive, 20.5 per cent; general lymph node tuberculosis, 4 per cent; doubtful, 6.8 per cent. The lungs are regularly secondarily infected from the nodes by rupture of a bronchial node into a bronchus. He agrees with Ravenel that infection traversing the intestinal mucosa can infect the lungs primarily. He says sufficient microscopic examinations were made to incline him to ascribe less importance, so far as frequency is concerned, to infection through the intestinal mucosa than to that through the throat; provided we may draw conclusions as to the point of infection from the localization of the process, or of the latent bacilli. In certain cases we cannot deny the possibility of hematogenous infection of glands, for these have an affinity for

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(1) Münch. med. Woch., 1904, No. 51.
(2) Journal Infectious Diseases, 1904, p. 140.

tubercle bacilli. He thinks it easily possible for infection to spread from lymph glands without the chest to those within, and for this to occur, either from the cervicals to the thoracic, or from the mesenterics up. The fact that the usual direction of lymph flow is one way does not prevent infection from traveling the other way.

In 736 autopsies on adults, 50.95 per cent had tuberculous lesions and 49.05 per cent were free from them. He agrees with Lubarsch that Naegeli's figures are too high. He thinks primary lymph node tuberculosis is frequent in adults. As to the probable route of infection of the lungs in adults he agrees with Ribbert and Orth that even in hematogenous miliary tuberculosis the later nodules may be the largest, and the later course of the lesions may be the same as ordinary pulmonary tuberculosis. His observations lend much weight to those of v. Behring, namely—that pulmonary tuberculosis can and frequently does follow earlier gland tuberculosis. He says that the cause then is to be sought in tuberculous foci in other organs, mainly the lymph nodes, and that the infection of the lungs occurs most likely by the way of the blood. He also believes that much more stress must be laid upon primary infection through the throat and the digestive tract than has been done.

Mesenteric Glands in Relation to Tuberculosis. As the result of a study of the glands in 70 cases of tuberculosis Rosenberger[1] concludes: (1) In all cases of active tuberculosis and in most cases of inactive tuberculosis the mesenteric glands are infective. (2) While the glands may not show gross lesions or bacilli they produce the disease in guinea pigs. (3) In 40 per cent of the cases in which Rosenberger found evidence of tuberculosis in the glands they produced the disease on inoculation. The infectivity of the mesenteric glands is probably shared by other glands throughout the body.

Endothelioma of the Pleura. Lewis[2] reports the case of a man who had an accumulation of thick chocolate colored sterile fluid in the left pleura. It was of 6 months' standing. It had been repeatedly tapped. The temperature ranged from 99 to 102°. The rib was resected and the pleura found greatly thickened and somewhat nodular. The diagnosis of endothelioma, rather than of pleuritis, was based upon a hypertrophy of the collagenic fibres, and the abundance of spaces interpreted as lymph spaces. These spaces were filled with endothelial cells and occasional giant cells of endothelial origin. Lewis quotes Bassoe as follows: Starting from inflammation it appears as if an impetus has been given the lining cells of the lymphatics to proliferate, and to alter their morphologic characteristics so as to simulate in many localities cylindrical epithelium and give to the lymph channels the appearance of gland tubules. Extension is by continuity of lymph channels. It occurs to the lung, bronchial nodes, diaphragm, peritoneum and skeletal muscles in the vicinity.

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(1) Amer. Jour. Med. Scien., July, 1905.
(2) Transactions Chicago Path. Society, April, 1905.

Aneurism and Arterio-Sclerosis Camac[1] gives a most critical analytical history of the lesions of arterio-sclerosis. He divides the subject into two periods. During the first the disease was considered local; during the second it was regarded as a local manifestation of a more or less general process. Passing from its historic aspects he studied the aortas of 103 domestic animals without discovering any evidence of aneurism. [The Editor has seen an aneurism in the thoracic aorta of an old polar bear. The animal died from rupture of the aneurism into a bronchus.] Horses frequently have aneurism of the superior mesenteric and abdominal aorta, due to a parasite—Strongylus armatus. The vessels of animals are somewhat more elastic than those of man, yet Camac thinks the probable explanation of their immunity from aneurism may be due to their immunity from syphilis.

Analyzing the 799 reports of autopsies made by Nicholl (practically all of the subjects having been under 4 years of age), he found one case of atheroma in a boy of 2½ and one case of endocarditis. There were 10 cases of congenital syphilis without vessel lesions. In autopsy reports on 340 cases of aneurism, only 5 were found under 10 years of age. This is offered merely as food for thought in con-

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(1) American Journal Medical Sciences, May, 1905.

nection with the etiology of aneurism. In 370 autopsies on aneurism cases Camac found syphilis mentioned as present in 34 and absent in 72. The same series reported the condition of the lungs in 98. Of these 16 had pulmonary tuberculosis.

Taking the reports of about 3,900 autopsies into consideration he thinks the disease about 4 times more prevalent among negroes than among whites. Camac concludes that arterio-sclerosis and atheroma have little to do with the occurrence of aneurism.

In the 370 aneurism autopsies already referred to, no mention is made of the condition of the arteries in 300. In 70, however, the condition of the arteries is particularly noted. In 6 arterio-sclerosis was present, in 64 it was absent. He notes that the primary and essential changes in arterio-sclerosis are in the *intima*—in aneurism in the *media.* A study of the distribution of arterio-sclerosis and of aneurism shows that they are not the same. For example, of 100 sclerosed vessels the radial was involved in 87 per cent, while aneurism rarely involves the radial. Generally speaking, the cerebral arteries show sclerosis in brain workers; the coronaries in hypertrophied heart, and the radials in laborers. There is not the same incidence in aneurism.

It is Camac's opinion that we must look elsewhere for the cause of aneurism and he thinks we have it in molecular physical changes in the elastic fibres of the media, probably due to primary changes in the vasa vasorum. Studying the physical properties of normal and sclerotic arteries and aneurism walls, Camac says to attain the greatest strength with a given amount of material, a cylinder should be constructed of layers the elastic coefficient of which gradually increases from within out. Now this is exactly the arrangement of the arterial wall. The main source of weakness in an aneurism wall is that it is composed practically of but one coat. Histologic study of the walls of vessels were made with negative results. The tissues were stained with elastic tissue stains. Tissues normal and arteriosclerotic were subjected to acetic acid 1 to 20 per cent for 24 hours in an incubator. Then fixed, hardened, cut and stained. Other tissues were similarly treated with

KOH 1 to 20 per cent (5 per cent and below was best), and then prepared for miscropic study. Neither the microchemical nor ordinary histologic methods having shown any structural changes in the elastic or other tissues of the media, Camac concludes that the structural weakness is due to molecular changes resulting in decreased resiliency of the wall.

Aneurism of the Heart Resulting from Gumma. Hall[1] reports 2 aneurisms in one heart developing in the wake of gummata. A gumma, irregularly nodular in appearance and .8 in. in diameter, projected into the right ventricle. Microscopic sections showed a vascular granulation tissue consisting of lymphoid and plasma cells, fibroblasts and giant cells lying in a "reticulum of structureless basement substance." The tissue showed great tendency to break down. The diagnosis was based upon the points noted, the presence of some phenomena in the neighboring tissues and the absence of tubercle bacilli. Microscopic sections of the wall of the aneurisms showed the same tissue as in the gumma.

ORGANS OF THE ABDOMEN AND PELVIS.

Necrotic Stomatitis in Calves and Pigs. Mohler and Morse[2] have studied various epidemics and endemics of so-called "calf diphtheria" and "pigs' sore mouth" in this country. The term diphtheria is unfortunate, as the disease is not diphtheria. It is due to Bacillus necrophorus, a non-motile polymorphic anerobe, inhabiting normally the intestinal tract of hogs and, in all probability, of herbivora. It is found also in manure. The disease is found principally in calves and pigs. The bacterium cannot infect through an intact mucosa or skin covering. It produces an intense necrobiosis followed by exudation and formation of false membrane. There is coagulation, necrosis and cheesy degeneration of various internal viscera. It is contagious, spreading between members of the same herd, but it travels slowly from herd to herd.

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(1) Transactions Chicago Pathological Society, April, 1905.
(2) Bureau of Animal Industry Bulletin, Nos. 6, 7.

Pathology of Gastric Carcinoma. Tabora[1] gives the results of his observation of more than 212 cases of carcinoma of the stomach in Riegel's clinic. He holds with Boas that carcinoma of the lesser curvature is as frequent if not more so than carcinoma of the pylorus. The symptomatology in these locations differs greatly. Pyloric carcinoma differs in its symptoms according to whether it is primary or whether it originates in an ulcer.

Carcinoma originating in an ulcer in its early stages and often throughout its course is accompanied by hyperacidity and continuous hypersecretion. On account either of the cicatricial contraction of the ulcer, the malignant growth itself, or spasm due to the hyperacidity marked motor insufficiency occurs early. Only late, if at all, is HCl decreased and thus lactic acid may be absent throughout the disease.

In the early stages of the primary pyloric carcinoma the stenosis is usually slight and HCl gradually decreases.

The author speaks very favorably of the Gluzinski method of estimating the relative HCl insufficiency. Gluzinski[2] proceeds as follows: The fasting stomach is emptied in the morning, then after a meal rich in albumin (2 hard boiled and finely divided eggs and 100-200 c.c. of water), and again after a testmeal. These are all done on the same day and if after one or two of these meals no HCl is found it speaks very strongly for the presence of a carcinoma, although the absence of HCl in the contents of the fasting stomach has not the slightest significance. Differing from ulcer-carcinoma—primary pyloric carcinoma early gives rise to the presence of the Oppler-Boas bacilli and lactic acid. Hemorrhages are common, but are not so profuse as those of the ulcer-carcinoma. It is in this variety of carcinoma that we have the typical "coffee-ground" vomit.

The subjective symptoms run parallel with the motor insufficiency, thus primary carcinoma is the "carcinoma of symptoms"; ulcer-carcinoma less so, and carcinoma of the lesser curvature least. As to the presence of

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(1) Deutsche med. Woch., 1905, Nos. 15, 16.
(2) Mittheil. Granzgebieten Med. u. Chir., 1902.

a palpable tumor ulcer-carcinoma is the earliest to show one, due to the infiltrated border of the ulcer, the perigastritis of the spasm. The primary growth is only palpable after it has reached some size.

Tabora holds that hypersection either continuous or alimentary is almost pathognomonic for ulcer-carcinoma.

Bockelman[1] has shown that the gastric mucosa in *carcinoma ex-ulcera* is similar to that in ulcus simplex and the parietal or oxyntic cells of the peptic glands are well preserved, while in primary carcinoma, these as well as the peptic cells are destroyed early, thus explaining the difference in the HCl secretion in the two conditions.

Differing essentially from the two conditions above is carcinoma of the lesser curvature. This in the great majority of cases is primary, as a rule achylia is present from the beginning.

The motility in the early stages is good, but later may be interfered with by the carcinoma cells infiltrating the muscular coats, or—what is more common—the growth produces a stiffness of the lesser curvature, thereby interfering with peristalsis. Lactic acid occurs even earlier in this form of tumor than in primary pyloric carcinoma.

The lesser curvature of the stomach being accessible only in gastroptosis a palpable tumor is not common, it is usually small and often overlooked.

Tabora thinks the decrease of HCl in carcinoma is due to two factors: (1) A mucous gastritis; (2) production by the carcinoma of basic substances which combine with HCl. Of course a carcinoma may occur in a stomach already the seat of achylia, and this condition even acts as a predisposing cause of the tumor.

Stagnation and subacidity are essential to the formation of lactic acid. The presence of this substance is of great diagnostic importance, its absence on the other hand is of little value.

Appendicitis Lesions in the Liver and Kidney. Beauvy and Chirie[2] report some cases of appendicitis with profound changes in the liver and kidney which they interpret as due to absorption from the appendix. Such cases usually die within a few hours after the onset of the attack, and no gross changes can be seen. It seems that Dieulafoy[1] had reported and classified several similar cases. Other observations quoted by them are: Quénu (Societe de Chir., Jan. 21, 1903), Morzard et Segonet (Soc. med. Hopitaux, Nov. 25, 1904), Bernard (Journal de Med., Paris, 1902), Barth (Soc. med. des Hop., 23 Oct., 1903), Moldawski (Wratch, XXII, p. 610), Renon (Bull. Acad. Medicine, 1898), and a great many others, some quite loosely joined in the grouping. The liver was found nearly wholly necrotic in these cases. The portal zones showed cells that are swollen and fatty. The protoplasm is reticular in appearance and feebly basophilic. In the subhepatic zone the cells look as though they were undergoing coagulation-necrosis. The cells are fragmented, stain deeply with eosin and the nuclei cannot be distinguished. In the kidney all the secreting portions show cloudy swelling and fatty degeneration and running together of the cells.

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(1) Zeitschrift f. klin. Med., 1902.

(2) Archives de Med. Exp. et d'Anatomie Path., March, 1905.

The lesions are held to be truly toxinic. A toxemia is not a competent explanation. It is due to the absorption of a poison eminently necrosing. They think the element of the closed cavity has much to do with the production of so violent a poison.

Relation Between Pathologic Processes in the Liver and Those in the Spleen. Levi Sirogue[2] says that the long known relationship between diseases of the spleen and liver has been explained on mechanical grounds, on the basis of compensatory hypertrophy, etc. Chauffard calls Banti's disease a hepatitis of splenic origin. Some of the reasons for this belief are: (a) Some cirrhoses are noticed secondarily to splenomegalies; (b) the blood of the spleen passes through the liver and not vice versa; (c) Chauffard and Castaigne were able to infect the liver through the spleen; (d) Kelsch and Kiener and Lesnè report several cases of spenomegaly due to malaria which were followed by cirrhosis of the liver.

Banti's disease has three stages: 1. Anemia, spleno-

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(1) Clinique de l'Hotel Dieu, 1898, p. 349, et Presse Medicale, July 9, 1902.

(2) Gazette des Hôpitaux, Feb. 25, 1903.

megaly, normal liver. 2. Anemia, splenomegaly, cirrhosis. 3. Ascites.

Gilbert and Fournier describe a splenomegalic hypertrophic cirrhosis. In this case the cirrhosis of the liver precedes the splenomegaly. The spleen changes are due to passive congestion. Boix reports a patient dying at 30 from cirrhosis of the liver who gave a history of splenic enlargement in childhood. Chauffard classifies the associated splenomegalies and cirrhoses as follows: (a) Splenomegalic form (simultaneous lesions in the two organs); (b) presplenomegalic form; (c) metasplenomegalic form.

Fat Necrosis Following Gunshot Wound of the Pancreas. Kindt[1] reports a gunshot wound of the abdomen with perforation of both walls of the stomach and the pancreas. At the operation 9½ hours later there were no signs of fat necrosis, the stomach wounds were sutured and the peritoneal cavity drained.

Four days later the patient died with the symptoms of general peritonitis and collapse. The autopsy showed no peritonitis, but the presence of a disseminated fat necrosis most marked in the vicinity of the pancreas. In the absence of any specific statement to that effect it is assumed the fat necrosis did not extend beyond the abdominal cavity. Microscopically the pancreas showed a more or less diffuse degeneration with scattered areas of fat necrosis.

Experimental Fat Necrosis. Hess[2] reports additional experiments to substantiate his theory of the cause of fat necrosis. He had previously shown[3] that fat necrosis may be produced by the injection of fat into the pancreatic ducts. This effect he attributes to the soaps formed by the action of the pancreatic juice on the fat.

To ascertain whether fat can enter a normal papilla of Vater from the duodenum, Hess ligated the duodenum below the entrance of the pancreatic duct, before and after the operation he introduced 150 c.c. of olive oil into the stomach. In no instance was fat necrosis produced.

In a second series of experiments he fixed a glass canula

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(1) Münch. med. Woch., 1905, No. 10.
(2) Ibid., 1905, No. 14.
(3) Ibid., 1903, No. 44.

in the duct and introduced oil into the stomach as before, but without success.

In a third series of experiments he fixed a canula in the duct as before, but in this series he also caused a stenosis of the duodenum by a ligature. Here he was able to produce a typical fat necrosis.

From these experiments Hess concludes: (1) That at least some of the cases of pancreatic fat necrosis originate from the entrance of fat-containing intestinal contents into the ducts of the gland. (2) That probably some cases of chronic interstitial pancreatitis are the result of healing of a previous necrosis caused by the entrance of intestinal contents.

Primary Carcinoma of the Ampulla of Vater. Moore[1] reports a case, and he thinks there are not more than 8 or 9 on record. It is difficult to distinguish carcinoma of the ampulla from carcinomas originating in the other ducts of this vicinity. In this case the emaciation, cachexia and jaundice were extreme. At autopsy a small glandular carcinoma was found at the juncture of Wirsung and the common duct. There was obstruction and consequent dilatation of the bile and pancreatic ducts. The notable point was the extreme emaciation consequent upon so small a tumor. The literature cited is: Devic and Gallvardin (Rev. de Med., 1901), Hanot (Archives Gen. de Med., 1896), Hall (Lancet, 1902, I, p. 1102), Halsted (Johns Hopkins Hosp. Bull., January, 1900) and Rolleston (Lancet, 1901, I, p. 467).

Chylous Ascites With Eosinophilia. Boston[2] reports a case of chylous ascites with an 8,000 leucocytosis of which 25 per cent were eosinophilia. Examination for trichina and other parasites was negative. Autopsy showed a limited tuberculosis. He collects 126 cases from the literature.

Relation of Nephritis to Hydramnion. Bruno Wolf has produced a marked increase in the amniotic fluid of animals by extirpating both kidneys.

Bibergil[3] has investigated the subject along a different line. By giving pregnant animals ¾ c.c. of 1 per cent solution of uranium nitrate with large amounts of water he caused a nephritis in the mother with serous effusions, and increase in the amniotic fluid, as well as nephritic changes in the fetal kidneys. Somewhat remarkable is the fact that the urine, exudates and amniotic fluid contained dextrose.

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(1) Journal Pathology and Bact., 1904.
(2) Jour. Amer. Med. Assn., Feb. 18, 1905.
(3) Berlin klin. Woch., 1905, No. 15.

Malignant Tumor of the Suprarenal. J. Dreschfeld and F. C. Moore[1] report a typical hypernephroma of the left suprarenal. There was metastasis to the lung and possibly the testis. They think metastasis occurs through the venous channels.

Vaginal Cysts. Cullen[2] reports on 53 vaginal cysts. His classification is as follows:

1. Inclusion cysts—due to inclusion of a small portion of the vaginal mucosa in the underlying tissue. These are relatively small and are principally in the lower lateral wall. They are usually due to tears. Sometimes they form globular masses on the posterior wall. They vary in size from ⅛ to 1 in. in diameter. The smaller ones are yellow, the larger white. They are frequently filled with exfoliated epithelial cells. The cyst wall is lined by squamous epithelium.

2. Cysts arising from vaginal glands. These cysts are less common, and 5 to 15 mm. in diameter. They are lined by cuboidal or cylindrical epithelium and contain mucus. They are generally in or near scars, and associated with one or more cysts of the first group.

3. Cysts of Gärtner's duct. These may be single or multiple. When multiple the cysts are in a row. While usually small they may reach several centimeters in diameter. They contain a clear straw-colored fluid. They are usually found in the anterior wall just behind the urethra. The cyst wall is smooth on the convex vaginal portion and undulating in the fixed portions. The epithelium is a single layer of cylindrical cuboidal or flattened cells. Cullen reports a Gärtner's duct cyst in the vaginal fornix.

4. Vaginal cysts arising from urethral glands. This

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(1) Journal Pathology and Bacteriology, November, 1904.
(2) Johns Hopkins Hosp. Bulletin, 1905.

is a very rare form. The lining epithelium is similar to that of the urethra.

5. Gas cysts. These are found principally during pregnancy. They are usually located in the submucous tissue though they may be in the mucosa. The mucosa is very apt to be hyperemic and succulent.

6. Echinococcus cysts.

NERVOUS SYSTEM.

Brain Tumor. Evans and Colver[1] have gathered several classified lists of brain tumors relating especially to the frequency of the different varieties. Starr's table of 600 cases shows tuberculosis, 30 per cent; glioma, 20 per cent; carcinoma, 8 per cent; and gumma, 4 per cent.

Another list of 100 gave the following as the rate of frequency: Glioma, 20 per cent; sarcoma, 18 per cent; tuberculosis, 13 per cent; gumma, 13 per cent; carcinoma, 7 per cent.

In Blackburn's report of autopsies on 1,814 insane patients 31, or 1.7 per cent, had tumor of some portion of the brain.

Schuster collected a large number of reports of cases and analyzed them especially as to the location of the tumor: 21.6 per cent were in the cerebellum; 14.7 per cent multiple; 12.1 per cent in the frontal lobes; 12 per cent in the motor regions, and 2.5 per cent were in the corpus callosum.

Hyperplasia of Chromophile Cells of the Hypophysis as the cause of Acromegaly. Lewis[2] says that in 96 per cent of the reported cases of acromegaly which have been followed by autopsy the hypophysis has been found enlarged. There are about 6 cases on record in which no changes were noted. The lesions of the hypophysis have been of all sorts; none has predominated, *e. g.*, simple hypertrophy, 2; adenoma, 7; sarcoma, 5; cystic tumors, 2, etc. On the other hand, there are many cases reported in which these same lesions were found in the hypophysis and acromegaly was not present.

Lewis accepts the opinion of Benda[3] that the essential

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(1) Amer. Jour. Med. Sciences, January, 1905.
(2) Johns Hopkins Hosp. Bulletin, May, 1905.
(3) Deut. med. Woch., 1901.

lesion in acromegaly is a proliferation of the chromophile cells probably indicating an excessive activity of the gland. He reports a case of very early acromegaly in which death was due to an intercurrent malady. To the naked eye the pituitary showed nothing. On microscopic examination he found proliferation of the chromophile cells. There was very little stroma. The gland was a mass of cells of two types, one small, round and compact, and another large, polyhedral with a vesicular nucleus. The granules stained with iron hematoxylin. Lewis thinks many of the cases reported as sarcoma were merely hyperplasias of these cells. He agrees with Benda that the hypophysis should be examined in all cases of death from goitre.

Open Areas in Central Nervous System. H. Schmaus[1] reports a case of flaccid paralysis of all four extremities, the spinal cord of which showed marked softening in the cervical region. On microscopic examination there was found about the central canal and in the ventral part of the posterior columns, round sharply defined clear areas in which the axis cylinders were still present, but denuded of their myelin sheaths. The ganglion cells in these areas showed a marked tigrolysis.

Clear areas in the central nervous system were first described in a case of multiple sclerosis by Borst, who considered them due to a lymph stagnation subsequent to an obstruction of the lymph channels somewhere between the perivascular capillary lymph channels and the pia-arachnoid space. Schmaus leans to the side of a chemical rather than a mechanical origin.

Histologic Changes of Peripheral Nerves in Cases of Chronic Edema. Dopter[2] says that in chronic edema of various origins (phlebitis, nephritis, etc.), some degenerative changes occur in the nerve trunk of the edematous region. This phenomena was first noticed by Klippel. The degenerative changes of the peripheral nerves are very similar to the Wallerian degeneration, which follows nerve division.

The author calls attention to the fact that the disintegra-

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(1) Münch. med. Woch., 1905, No. 12.
(2) Gaz. des Hôpitaux, Jan. 12, 1905.

tion of myelin begins at the node of Ranvier and spreads to the entire segment of myelin. Ranvier has shown that this node is the only portion through which nutritive substances can penetrate into the internodal segment.

The edema fluid is only slightly toxic, and the changes are not due to the toxicity, but merely to its presence and prolonged contact. Ranvier was able to cause changes in the sciatic of a rabbit by keeping the nerve in contact with normal salt solution for several hours.

The edema fluids dialyse through the nodes of Ranvier and invade the myelin, which becomes disintegrated.

Conclusions:

1. The motor and sensory changes or derangements in chronic edema are due to anatomic changes in the peripheral nerves.
2. The changes are of two types: (a) Wallerian degeneration; (b) "periaxial segmentary necrosis."
3. The "periaxial segmentary necrosis" is due to the penetration of Ranvier's node by the surrounding fluids, which finally invade the internodal segments, destroying the myelin, but—relatively—respecting the axis cylinder.
4. If the axis cylinder is involved, interfering with transmission of impulses, the changes are of the Wallerian type.

LOCOMOTOR SYSTEM.

Carcinomatous Osteomalacia. Woodyatt[1] reports the case of a woman with such extensive secondary involvement of the bones with carcinoma as to deserve the title carcinomatous osteomalacia. While secondary carcinoma of the bones subsequent to carcinoma of the mammary gland, prostate and thyroid is not unusual, diffuse carcinomatous infiltration of the bones with softening has only been reported in 7 cases that he could find.

It would appear that Handley (Lancet I, 1905, i, p. 909) quotes Paget (Lancet, March 23, 1887) as having collected 14 cases, though the text referring to these does not make it clear that the carcinoma diffusion was widespread. Woodyatt's case was in a woman from whom a mammary

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(1) Trans. Chicago Path. Society, June 12, 1905.

carcinoma had been removed three years previously. There was return in the scar. He says all bones examined showed diffuse displacement of the bone by a soft whitish tissue. The softening resulted in very extensive deformities. The process was uniformly osteomalacic in type. He cannot agree with Rokitansky that on the hyperemic side of a carcinoma focus there would be an osteoblastic process, whereas on the other, or anemic, side there would be an osteomalacic process.

He quotes Bruns as having studied 71 cases of metastatic bone carcinoma, and as having found the mammary gland the primary site in 59.

Handley (loc. cit.) says that at Middlesex Hospital from 1872 to 1901 they have had 329 cases of mammary carcinoma going to fatal termination. Of these there was involvement of the sternum in 30; ribs, 28; clavicle, 5; spine, 12; cranium, 9; scapula, 1; femur, 14; humerus, 9; tibia, 1; patella, 1; bones of hand, 1.

Petrèn[1] describes 3 cases of involvement of pelvic bones secondary to mammary carcinoma. In one of these 7 to 8 years had elapsed between the removal of the original carcinoma and the recurrence. Every author writing on the subject believes the bones are involved far more frequently than is generally thought. Spontaneous fracture is usually the reason for examination of the bones, and such accident is only prone to occur in the long bones. Such cases as that of Petrèn and one reported by Sette[2] in which there was an involvement of the posterior fossa of the base of the skull are significant.

Paget, collecting 650 cases of fatal mammary carcinoma, found spontaneous fracture of the femur or a plain focus therein in 18; of the humerus in 10; and of the cranium in 36.

Gallvardin and Varny[3] state that about 50 per cent of carcinomas of the brain are secondary to mammary carcinoma.

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(1) Grenzegebiete der Med. u. Chir., 1905, p. 505.
(2) Rev. Veneti di Sciences Med., 1905, XLII, 108.
(3) Rev. de Med. Paris, July, 1903, and Pract. Med. Series, 1903, Vol. IX.

Dick[1] reports a *myeloma* of the cranium involving the left frontal bones. The cells were mostly of the small variety described by Wright.

Experimental Streptococcus Arthritis. Cole[2] says that it is his custom to inoculate tubes from the blood in every case of acute articular rheumatism, and from the joints in all those cases in which there is any fluid. These examinations have always proven negative. He quotes Philipp[3] as having had a similar experience. He obtained streptococci from many different sources and inoculated them intravenously into animals. Arthritis and endocarditis were uniformly produced. He concludes that the lesions can be produced by many different cocci. He does not assume to decide whether such organisms are the cause of acute articular rheumatism or not.

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(1) Trans. Chic. Path. Society, June 13, 1904.
(2) Journal Infec. Dis., November, 1904.
(3) Deut. Archiv f. klin. Med., 1903, p. 152.

SECTION IV.

BACTERIOLOGY.

A revision of the coccaceæ is proposed by Winslow and Rogers.[1] The following is the classification presented:

FAMILY COCCACEAE.

Vegetable cells spherical.

Subfamily 1. PARACOCCACEAE (*new subfamily*).

Parasites (thriving only, or best, on or in the animal body). Thrive well under anaerobic conditions. Many forms fail to grow on artificial media, none produce abundant surface growths. Planes of fission generally parallel, producing pairs, or short or long chains.

Genus 1. *Diplococcus* (Weichselbaum).

Strict parasites. Not growing or growing very poorly, on artificial media. Cells normally in pairs, surrounded by a capsule.

Under *Diplococcus* are three species, *D. pneumoniae,* Weich., *D. Weichselbaumii,* Trev. and *D. gonorrhoeae,* Neisser—distinguished by the tissue of the host affected, and by the peculiar morphology and staining reactions of the latter species.

Genus 2. *Streptococcus* (Billroth).

Parasites (see above). Cells normally in short or long chains (under unfavorable cultural conditions, sometimes in pairs and small groups—never in large groups or packets). On agar streak effused translucent growth often with isolated colonies. In stab culture, little surface growth. Sugars fermented with formation of acid.

Under *Streptococcus* we find the vast majority of organisms indistinguishable from *S. erysipelatos,* Fehleisen. Two

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(1) Science, April 28, 1905.

varieties may perhaps be recognized, var. *involutus* Kurth; and var. *tenuis* (new variety), which fails to coagulate milk. Representatives of another species, *S. enteritidis* Escherich, which liquefies gelatin, are occasionally found.

Subfamily 2. METACOCCACEAE (*new subfamily*).

Facultative parasites or saprophytes. Thrive best under aerobic conditions. Grow well on artificial media, producing abundant surface growths. Planes of fission often at right angles; cells aggregated in groups, packets or zoöglea masses.

Genus 3. *Micrococcus* (Hallier) Cohn.

Facultative parasites or saprophytes. Cells in plates or irregular masses (never in long chains or packets). Acid production variable.

Under this genus, thirteen species may be distinguished, by the three properties of liquefaction, acid production and chromogenesis, their characters being indicated in tabular form below.

GELATIN LIQUEFIED.

	ACID.	NON-ACID.
Yellow..	*M. aureus* (Ros.) Mig.	*M. orbicularis* (Revenel).
White..	*M. pyogenes* (Ros.) Mig.	*M. rhenanus* Mig.
Red....	*M. roseus* Flügge.	*M. fulvus* Cohn.

GELATIN NOT LIQUEFIED.

	ACID.	NON-ACID.
Yellow..	*M. luteus* (Schroter) Cohn.	*M. ochraceus* Rosenthal.
White..	*M. candicans* Flügge.	*M. canescens* Mig.
Red....		*M. cinnabareus* Flügge.

Genus 4. *Sarcina* (Goodsir).

M. ureae Cohn. Ammoniacal fermentation of urine produced. Gelatin not liquefied.

M. aethebius Trevisan. Ammoniacal fermentation of urine produced. Gelatin liquefied.

Saprophytes or facultative parasites. Division under favorable conditions, in three planes, producing regular packets. Sugars as a rule not fermented.

Under *Sarcina* are eleven species, eight of which are grouped as follows:

	GELATIN LIQUEFIED.	GELATIN NOT LIQUEFIED
Yellow	*S. subflava* Ravenel.	*S. ventriculi* Goodsir.
White	*S. candida* Lindner.	*S. pulmonum* Virchow.
Red	*S. rosacea* Lindner.	*S. incarnata* Gruber.
Brown	*S. cervina* Stub.	*S. fusca* Gruber.

In addition three somewhat aberrant species must be recognized—*S. aurantiaca* Flügge, a yellow liquefying chromogen, which, unlike the other members of the group, has the power to coagulate milk, with *S. agilis* (Ali-Cohen) Mig. and *S. tetragenus* (Mendoza), Mig., respectively red and yellowish-white, motile forms. From study of the literature and a few cultures of supposedly motile forms we are inclined to believe that all the truly motile cocci may be classed under these two heads.

Genus 5. *Ascococcus* (Cohn).

Generally saprophytic. Cells imbedded in large, irregularly lobed masses of zoögloea, in presence of carbohydrates. Acid usually formed.

Two species are distinguished, *A. mesenteroides* Cienkowski, a non-liquefying form, and *A. mucilaginosus* Migula, a liquefier.

Resistance of Bacteria to Desiccation. Reports of experiments by Heim[1] give the following as the lengths of time that bacteria were cultivated from the materials as noted:

	Year.	Month.
Tetanus bacilli in pus over	2	..
Tetragenus in mouse blood	2	..
Typhi muri in mouse blood	1	10
Diphtheria bacilli on serum	1	11
Xerosis bacillus on agar	1	8
Staphylococci in pus from knee	1	4
Streptococci from peritonitis	1	4
Anthrax in guinea-pig blood	2	5

In all other instances the bacteria, as tetanus and anthrax, were free from spores. The specimens were mostly

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(1) Zeit. f. Hygiene, Bd. L., Heft. 1.

smeared onto threads, and then laid on sheets of glass, where they dried. These glass plates with the threads were then carefully put away.

Copper and Bacteria. The observations of Pennington[1] show that copper plates electrically charged have a germicidal action against typhoid and colon bacilli in water. Larger plates have a more positive action, and it would seem the effect is due to coming in contact with the electrified surface rather than to any particular amount of copper in solution in the water.

Blank Cartridges. Experiments on blank cartridges appear from time to time. Dolley[2] reports results at some variance with previous observations, which rather tend to show that tetanus comes from bacilli in dirt on the hands and clothing. The author comes to the following conclusions: *B. ærogenes capsulatus* was present in a large proportion of the wads of Peters, U. M. C., and Winchester makes. The Peters wads, when inoculated in animals, produced characteristic symptoms of tetanus. The powder of the three brands was negative for *B. tetani* and *B. ærogenes capsulatus.* Attempts of the writer to isolate *B. tetani* from wads were unsuccessful. There is clinical evidence and animal experiment results sufficient to demonstrate the presence of *B. tetani* in wads.

Intracellular Toxins. The article by Vaughan[3] deals with intracellular toxins and is a continuation of the work he has had in hand for several years, and of which we have previously reported in part. By acting upon the cell with sodium alcoholate the writer has recently been able to split off and obtain in soluble form a highly poisonous group. This was done with the colon, typhoid and anthrax. Antibodies for these toxins were also made. In regard to the colon toxin, this—as obtained—seems to be the specific toxin, as it immunized guinea-pigs. In these animals injections of the toxin cause a fall in temperature, whether fatal or non-fatal doses are given. If the injection is made into the peritoneal cavity, the temperature

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(1) Amer. Jour. Med. Sci., May, 1905.
(2) Jour. Am. Med. Assoc., Feb. 11, 1905.
(3) Jour. Am. Med. Assoc., Sept. 3, 1904.

falls, and even if it reaches as low as 95° F., and ceases to fall, the animal will recover. In any case the moment of change to recovery is thus indicated. When the sterile germ substance is injected intraperitoneally a hemorrhagic peritonitis is the result, but when the split-off toxin is injected, no disturbance of the peritoneum is noticed. Recovery is apparently complete in two to three hours.

The conclusions that may be drawn from this investigation are:

1. The colon bacillus, in its essential part, is a chemical compound as truly as sodium sulphate. This is proven by: (*a*) that when treated with dilute acid the body split from the germ is uniform quantitatively and qualitatively, whether 0.1 or 1 per cent is used. (*b*) The germ substance has a definite chemic composition, and cleavage occurs along a definite line under the influence of acid. The groups having different properties are in combination, and are not extracted by solvents, but are only separated by agents which split up molecules.

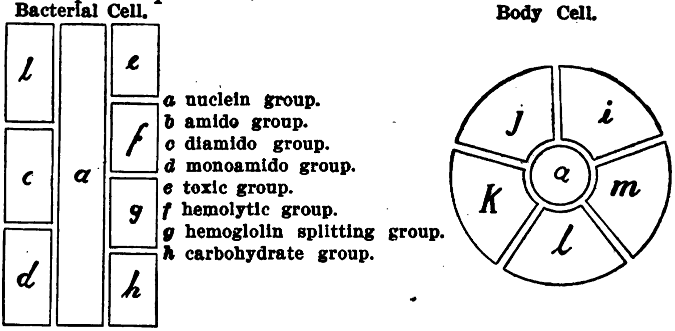
2. The colon bacillus is a chemical compound having the following groups: Nuclein, amido, diamido, monoamido, carbohydrate, toxic, hemolytic and hemoglobin splitting.

3. Every cell in the animal body contains complex molecules similar to those in the bacillus.

4. The reaction between the colon molecule and a body molecule or cell is chemical. When two such molecules are brought into relation, such groups will be split off from either to fulfill the reaction, and the damage done will be in proportion. The stability of the molecule's integrity must be overcome. This can be seen in the action of colon cell substance and the split-off toxin group. In the first instance 10 to 24 hours are required for liberation of the toxin group so that its poisonous effect may be seen, but if the split toxin is injected, its poison effect may be seen in as many minutes.

5. The production of antitoxin takes place by the repair of the body cell in replacing the atom groups that have been lost. When these are in excess they are expelled and become free. This would follow after Ehrlich's theories.

Graphic representations:



a nuclein group.
b amido group.
c diamido group.
d monoamido group.
e toxic group.
f hemolytic group.
g hemoglolin splitting group.
h carbohydrate group.

Mechanism of Agglutination. The theories that have been advanced by various writers regarding the cause of agglutination phenomena are discussed by Craw.[1] The writer does not consider the theories so far presented explain all the facts. Pfeiffer's and Emmerich's proposition that bacteriolytic enzymes cause the vital paralysis, and that of Gruber, Dineur and Nicolle, which ascribes the action to the glutinous nature of the membranes or cilia, are untenable because of experiments with heated cultures and sera. Heating to a temperature which destroys enzymes does not affect agglutinins. The views of Paltauf and Ducleaux, that a specific precipitate is formed which mechanically carries the bacilli together, would be sufficient were it not for certain results with washed bacilli.

That visible precipitates can cause agglutination is certain, but the degrees of agglutination activity do not go hand in hand with the development of precipitation. He does not consider that the gas laws as proposed by Arrhenius can be applied here, because there are no conditions warranting their introduction into the question.

The agglutinable substance is evidently within the cells, as washed cell capsules are but slightly agglutinated. Motile cultures grown at 98.6° F., and non-motile cultures grown at 107.6° F., agglutinate equally well; the agglutinins are evidently unchanged. The laws relating to the fixation of *B. typhosus* heated to 136.4° F. are evi-

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(1) Jour. f. Hygiene, 1905, No. 1.

dently different from those of living cultures, probably because the agglutinable substance is changed.

Agglutination; Relation of Flagella. The part played by flagella in the phenomena of agglutination will not hold, but that it is more likely to be a physical pheena has been studied by dé Rossi.[1] Flagella were mechanically separated from bacteria and tested individually. He found the same degree of agglutinative power could be obtained whether animals were injected with flagella or with bacilli. There does not seem to be an elective action for one or the other; that is, one can not recognize a "cilioagglutinin" and a "somatoagglutinin." However, flagella absorb agglutinins much more actively than bacillus bodies. It does not matter how the serum was prepared; but a suspension of flagella added to such sera caused a more rapid and complete removal of agglutinins than did either entire bacilli or bacillus bodies alone. There does not appear to be any special property causing the formation of agglutinins, but there is a special ability to fix the same by flagella. During or after agglutination of motile organisms the flagella remain attached to the cells and show no change in form or numbers.

The writer considers that the results of his observations show that Gruebler's theory—changes in cell wall—will not hold, but that it is more likely to be a physical phenomenon, as proposed by Bordet. From a practical standpoint it would seem necessary to study agglutination phenomena on normal living organisms in order to recognize all its phases.

Agglutination Due to Gelatin. A number of observers have noted that gelatin can induce agglutination of motile bacilli. Weil,[2] in a closer study of this subject, finds that gelatin acts upon the agglutinable bacterial substance in the same manner as a specific serum. The action is upon the receptors or haptophore group of the cells. It was found that gelatin, like a specific serum, was bound or used by the bacterial cells. The only difference between the two is in the absence of a specific action upon the part of gelatin. The writer considers that crystalloids—probably calcium salts—have much to do with the reactions.

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(1) Zentr. f. Bakt., XXXVII, Heft. 1,

(2) Ibid., XXXVII, Heft 3,

Gelatin cannot be made inactive through heating, as is possible with specific sera.

Bacteriology of the Intestine. Hewetson presents the 8th report on the bacteriology of the intestine and inflammatory processes arising therefrom. The writer made both ærobic and anærobic cultures. In non-suppurative cases of appendicitis he found the appendix completely stenosed in 25 out of 44 cases. The closed end was sterile in 11, and showed cultures in 14. The organisms found are stated as:

Bacillus coli alone in 11.
Bacillus coli and a torula in 1.
Staphylococcus pyogenes aureous in 1.
A streptobacillus in 1.

In non-stenotic cases the results showed:

Bacillus coli alone in 16.
Bacillus coli and Staphylococcus albus in 1.
Streptococcus pyogenes in 1.

Six of the cultures of B. coli were found virulent for rats by peritoneal injection.

In the study of suppurative appendicitis presented, a special point is made of the possibility of organisms dying in the pus before evacuation. In two instances the pus around the appendix was found sterile. As to the frequency of organisms, the results were:

Bacillus coli in 34.
Micrococci in pairs and chains, 18.
Streptococcus pyogenes in 7.
Diplococci in 5.
Bacillus pyogenes in 5.
Pneumococcus-Frænkel in 2.
Diplobacillus in 1.
Actinomycosis in 1.

B. coli was most abundant, and was found virulent in the five cases tested. The work of Rist[1] could not be verified by the writer, in that he found the anærobic organisms described by Rist to be facultative when properly cultivated. Purely anærobic organisms do not seem to have an important place in this connection.

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(1) Brit. Med. Jour., Oct. 12, 1901.

In abdominal suppuration of doubtful origin the bacteria isolated in 6 cases were:

Bacillus coli in 2.
Streptococcus pyogenes in 2.
Pneumococcus-Frænkel in 1.
Staphylococcus pyogenes aureus in 1.
Actinomycosis in 1.
Micrococci in 1.
An unknown coccus in pairs in 1.

The cultures made from the biliary passages were made in the operating room, and showed of 19 cases, 3 were sterile and—

Bacillus coli was isolated in 8.
Micrococci in 5
Streptococcus pyogenes in 4.
Cocci, unknown, 3.
Bacillus subtilis, 2.
Bacillus typhosus in 1.
Staphylococcus aureus in 1.
Torula in 1.
A minute bacillus in 1.

During operations on the stomach and jejunum cultures were made, and of 36 cases, 18 were found sterile. The percentage of sterility was:

In cancer of esophagus:
  Stomach sterile in 50 per cent.
In gastric dilatation, without ulceration:
  Stomach sterile in 83 per cent.
  Jejunum sterile in 82 per cent.
In gastric dilatation with ulceration:
  Stomach sterile in 28 per cent:
  Jejunum sterile in 40 per cent.

The viscera were empty in all of these cases and the patient had been fasting for some hours. In those cases showing growths the following organisms were isolated in the order presented:

Stomach.

Torula in 7.
Streptobacilli in 3.
Bacillus coli in 3.

Micrococci in 3.
Streptococcus pyogenes in 3.
Bacillus subtilis in 2.
Staphylococcus albus in 2.
Sarcinæ in 2.
Bacillus proteus in 1.
A minute bacillus in 1.

Jejunum.

Staphylococci in 5.
Bacillus coli in 3.
Torula in 2.
Streptococcus pyogenes in 1.
Sarcinæ in 1.
Bacillus subtilis in 1.
Bacillus proteus in 1.

From the results obtained, the writer suggests it is not necessary to wash out the stomach to the extent usually done, because of the few organisms found when it becomes empty. In 4 cases of perigastric and periduodenal suppuration there were found:

Bacillus coli in 2.
Micrococci in 2.
Streptococcus pyogenes in 1.
Large coccus in 1.
Bacillus subtilis in 1.
Actinomycosis in 1.

The question of food in the stomach was also studied, and the conclusion reached that the introduction of either food or sputum at once increases the numbers and varieties of bacteria in that organ.

Bacteriology of Prostate. Dudgeon and Wallace[1] examined 7 enlarged prostates and found 3 infected with Staphylococcus albus, and 2 with B. coli. As the urine usually contained the same bacteria, the writers conclude that in most instances infection takes place from bacteria present in the urine and bladder.

Surgical Infection from the Skin. In an important arti-

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(1) Brit. Med. Jour., Dec. 31, 1904.

cle Collins[1] presents his experiments as to methods of sterilizing the skin, and especially the hands of surgeons. He finds the following relative values of antiseptics used:

	—Length of time—		Carbolic acid co-efficient.
Antiseptic—	1 minute.	5 minutes.	
Carbolic acid	1-50	1-100	1.
Lysol	....	1-100	1.
Cyllin	1-600	1-1,250	12.5
Perchlorid of mercury	1-2,500	....	50.
Mercuric potassium iodid	1-4,000	1-8,000	80.
Formalin	....	1-30	.3

The method of experiment adopted consisted in having the hands cleaned, nails trimmed, washed with nail brush and soft soap in hot water containing some antiseptic. The time given here was ten minutes. They were then soaked in a different antiseptic for two minutes, dried on sterile gauze. The hands thus prepared were at once plunged into a jar containing one liter of nutrient peptone-broth with a layer of sea sand or marble dust at the bottom. The hands were well rubbed with the sand for five minutes, and at the end of that time the jar was covered and incubated. Sterile cloth was placed about the arms over the mouth of the jar during the washing process.

Results indicating sterilization of the hands were obtained by using cyllin in 1:600 in hot water for 10 minutes, followed by mercury perchlorid 1:2000 for 2 minutes. This group of results indicated that the skin can be sterilized, but in order to further prove the importance of bacteria in the sweat glands and follicles, another series of tests was made.

Pilocarpin was given in doses of 0.2 gr. and the hands with the resulting sweat were tested. The results here were only satisfactory when cyllin was used for 20 minutes and followed by mercury perchlorid 1:2000 for 2 minutes.

The use of alcohol is discussed by the writer, who states he finds in it an agent that simply dehydrates and fixes the skin with all contained bacteria, and considers that more damage is done by its use than good. Altogether his experiments are good, but do not cover enough kinds of antiseptic agents to warrant conclusions as to the most satisfactory method. The culture part of the investigation is very precise, and would certainly justify the assertion that the skin of the hands can be sterilized.

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[1] Brit. Med. Jour., July 15, 1905.

Anthrax: Natural and Artificial Immunity. Pettersson[1] compared the findings in normal animals and in those treated with anthrax cultures. The difference between the two, as already shown by Metchinkoff, is noticeable in the leucocytes. However, as regards his studies, the leucocytic activity is the sole reason for immunity. The writer finds in the extracellular lymph of the peritoneal cavity considerable evidence of bacterial disintegration. The activity of the leucocytes in destroying bacilli is much less in salt solution than when in serum, thereby indicating the great importance of complements in this connection. When dogs are immunized the result of the infection is in a great increase in the complements. Blood serum alone is inactive both before and after immunization. Specific antibodies do not seem to be formed by the treatment. Both in the natural animals and in those immunized, the chief agency operative in defense is complement. In many other animals the complement action is also of importance. There is more leucocytosis in the specially immunized dog than in the ordinary animal.

Anthrax: Serum Treatment. Lockwood and Andrews[2] used the serum prepared by Schard on a case of anthrax infection, with good success. A culture diagnosis of B. anthracis was made. The lesion was on the right cheek; 40 c.c. of serum were injected. For two days there was apparently no effect, when marked improvement took place, the bacilli disappeared, and the lesion finally healed completely.

Bubonic Plague: Bacteriologic Diagnosis in Rats. This has been a subject of special interest in the Hygienic Institute at Hamburg. Dunbar and Kister[3] discuss this sub-

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(1) Zentralb. f. Bakt., 1904, No. 1.
(2) Brit. Med. Jour., Jan. 7, 1905.
(3) Zentralb. f. Bakt., 1904, No. 1.

ject and present pictures of the bacilli isolated. The greatest difficulty in this connection is the mixed infection of the cadavers with organisms pathogenic for rats and guinea-pigs. At times there are found in the organs of such rats bacilli resembling B. pestis. The examination of these in hanging drops will often show they are motile. Another point of great value is the cutaneous inoculation

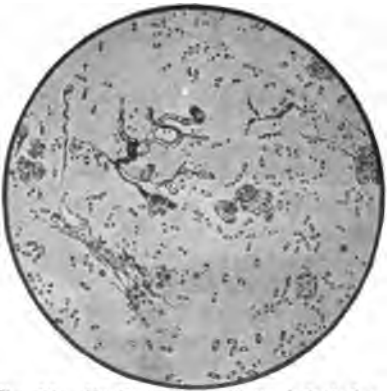

Fig. 13. Bacillus Pestis from infected rat.

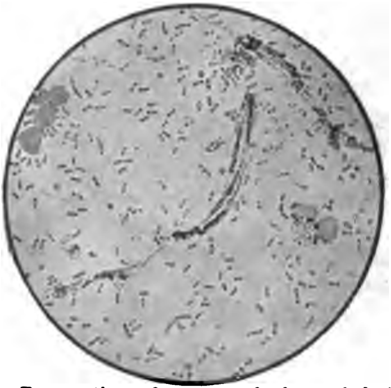

Fig. 14. Preparation of organs of plague infected rat.

of rats and guinea-pigs, thus avoiding the toxicogenic mixed infection.

In a study of *mixed infection in plague,* Goss[1] reports on the relations of B. pestis and M. pneumoniæ in cultures and animal experiments, as regards mixed infections in cases of the pneumonic form of plague. When grown together the pneumococcus retards the growth of plague because of acid production, but later, the alkali produced by the plague bacilli changes the reaction and they grow abundantly. In old cultures pneumococci die out because of the excessive alkalinity. When guinea-pigs and rats are inoculated with both cultures the two infections progress independently. Pneumococcus infection is more rapid, and may kill the animal some time before it would have died of plague. It was noted that the pneumococcus did not change the virulence of plague bacilli.

Etiology of Hog Cholera. Dorset, Bolton and McBryde[2] state great care must be taken in recognizing cases of hog cholera. They consider that the particular cases in hand must show infectiousness by contact, transmissibility through inoculation of blood or other tissue, and the evidence of immunity after recovery. The writers take this ground because these manifestations are seen in the natural course of epidemics. The results of inoculation experiments show conclusively that the blood of infected animals will transmit the disease. The bacteriologic condition of the blood of infected animals, both before and after death, was exhaustively studied. It was not possible in all instances when the blood proved infectious to isolate B. choleræ suis. Other bacteria were not found with sufficient regularity or numbers to count as etiologic factors. The writers filtered blood from infected animals through germ-proof porcelain filters, and found that it was still infectious upon being injected. At the same time these filtrates were also proven free from B. choleræ suis by cultures. The conclusion is clear that hog cholera is not due to B. choleræ suis and that it is capable of passing through a porcelain filter. Experiments with B. choleræ suis cause certain clinical manifestations that to some extent resem-

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(1) Arch. des Sciences Biol. (St. Petersburg), 1904, No. 5.
(2) Bureau of Animal Industry, Bulletin 72.

ble hog cholera, but which do not show the peculiarity of contact transmission and immunity after attack.

McClintock, Boxmeyer and Siffer[1] report *experiments on hog cholera.* They find that the serum reactions obtained with B. choleræ suis and the blood of normal hogs take place in dilutions of 1:100, 1:200 and even at times in 1:250 dilution. Reactions obtained with the blood of hogs naturally infected with hog cholera, and with that of those experimentally immunized, do not differ much from this, and indicates there is little diagnostic value to the serum reaction in this disease. The examination of a considerable number of hogs with hog cholera showed there was much variation in the limits of reaction; but that in those animals where B. choleræ suis was found, the reaction limit ranged from 1:600 to 1:2000. It rose in one hog to 1:50,000 during experimental inoculation, but in others it was low, seldom passing over 1:1200. In some no effect in this respect was noticed. As a rule, intraperitoneal injections gave the best results in increasing the serum activity, but here again there was no relation between the result achieved and the amount of culture used.

Previous to the Bureau of Animal Industry report the writers had sought another cause for the disease. This was because they were unable to find the organism in a number of typical cases; because the serum of some animals was inactive, and because they were unable to induce the peculiar lesions of hog cholera by injections of B. choleræ suis, or by feeding experiments. They repeated the experiments of the Bureau. A sick hog was selected and slaughtered. In the organs of this animal a bacillus resembling the hog-dysentery bacilli of Smith was found. The liver and spleen were fed to a second hog, which became infected and later was killed. The blood was filtered, and proved free from B. choleræ suis by cultures. This was injected intraperitoneally. This animal was infected, and the experiment was repeated four times in similar manner. At the same time the filtrates were found bacteria-free by cultures. It would seem, therefore, that the causal agent in this disease is like that of foot and

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(1) Jour. of Infectious Diseases, II, No. 2.

mouth disease, in being able to pass through a porcelain filter.

Diphtheria. The following results of examination of throat cultures in the Health Department Laboratory, Chicago, during 1904, are reported by Biehn:[1]

During the year 1,381 cultures were examined for suspected diphtheria.

		Per Cent.
373	contained Diphtheria bacilli	27.09
287	contained Streptococci	20.78
998	contained Staphylococci	72.26
375	contained Influenza bacilli	27.15

Clinical diagnosis *Diphtheria;* 364 showed:

		Per Cent.
133	contained Diphtheria	37.08
60	contained Streptococci	16.48
251	contained Staphylococci	68.95
86	contained Influenza	23.62

Clinical diagnosis *Tonsillitis;* 416 showed:

		Per Cent.
68	contained Diphtheria	16.34
79	contained Streptococci	18.99
290	contained Staphylococci	69.71
109	contained Influenza	26.20

Clinical diagnosis *Not Given;* 601 showed:

		Per Cent.
170	contained Diphtheria	28.20
148	contained Streptococci	24.62
457	contained Staphylococci	76.03
180	contained Influenza	29.95

Giersvold[2] reports *finding diphtheria bacilli* in the throats of 9.2 per cent of children presumably healthy, of 967 examined. (This examination was made in the spring months.) For a period in the fall 178 children were examined, and 3.4 per cent were found with bacilli. No child had any clinical manifestations, nor were there cases of diphtheria at home.

The *direct examination of smears for diphtheria bacilli*

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(1) Trans. Chicago Path. Soc., April 10, 1905.
(2) Tidsskrift f. d. Norske Laegeforen, 1903, No. 23.

is recommended by Highley,[1] who, with a strong flattened platinum loop, scrapes the surface of the tonsil. The material so scraped away is mixed in water and a thin even film is prepared. Kuehne's methylen blue, diluted, is applied for 5 seconds, and then dilute Ziehl's stain for 1 minute. The preparation is then to be washed and finished. The diphtheria bacilli may be easily recognized by their irregular outline, by the granules and by the dark red or violet stain they have taken.

Knapp[2] used the fermentation test to show the *differentiation of pseudo-diphtheria, B. diphtheriæ and B. xerosis.* He finds some difference in activity when the test is made using the serum-water mixture of Hiss. He prepared the media as follows: 1 part water and 3 parts beef serum are mixed and heated at 104° F. for a few minutes. This mixture is practically sugar-free. To portions are now added 1 per cent of dextrose, mannite, maltose, lactose, saccharose and dextrin. The solutions are now colored with a c. p. 5 per cent solution of litmus. After filling into test tubes it is sterilized by the fractional method.

In these media the results shown in 24 to 48 hour incubation are:

Pseudo-diphtheria bacilli do not ferment at all, and the media remain blue.

Diphtheria bacilli cause fermentation of dextrose, mannite, maltose and dextrin, the media turning red. Saccharose is not fermented.

Xerosis bacilli ferment dextrose, mannite, maltose, saccharose, with formation of acid and red reaction. Dextrin is not fermented. This bacillus also formed a surface pellicle.

Petrie[3] attacks the question of the *relation between B. diphtheriæ* and *pseudo-diphtheria bacilli* (Hoffmann's bacillus) in a new way. This is by adding quantities of pseudo-diphtheria filtrates to toxin-antitoxin mixtures, and by treating horses with large quantities of the filtrates, then examining the serum for antitoxin. Eleven strains of pseudo-diphtheria bacilli were used. These cultures

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(1) Medical Record, April 1, 1905.
(2) Jour. of Medical Research, November, 1904.
(3) Jour. of Hygiene, 1905, No. 2.

gave as characteristic findings: positive to Gram's stain, but no granules by Neisser's method. They gave an alkaline reaction when grown in glucose broth. Slides from cultures in alkaline bouillon for four days showed short parallel arranged rods when stained by Loeffler's stain. Involution forms were seldom seen. The injection of 5 c.c. bouillon cultures subcutaneously into guinea-pigs gave no result beyond an occasional slight local irritation.

It was shown in the first series of experiments that no substance capable of neutralizing diphtheria antitoxin is present in the filtrates from cultures of these bouillons. The experiments on horses were also negative, as even the injection of large quantities of the filtrates was incapable of stimulating the formation of diphtheria antitoxin. The presence of toxoids was also disproven. The difference between the organisms is therefore accentuated, and doubt is thrown on the possibility of their standing in any close relation. Clinically the question is of importance as showing that the Hoffmann bacillus, when present, cannot cause a neutralization of antitoxin used in the treatment of the case.

Van Calcar[1] presents experiments that demonstrate the presence of toxins. By dializing diphtheria toxins he finds that the toxin passes through first; *i. e.*, the dialized portion is toxic, while the remaining part is only capable of causing paralysis. The relative size of the atom groups is considered as causing the difference in dialization. It would appear from this result that the existence of Ehrlich's toxon group was definitely established. Toxons combine with antitoxin, but do not have the poisonous properties of the toxins. The writer also reports some experiments on the conditions developing in toxin-antitoxin mixture injected into the peritoneal cavity of animals which later recovered. These also would show that Ehrlich's views on the presence of multiple poison groups in diphtheria toxin are true.

Roemer[2] repeated Calcar's work to check his results. His apparatus was one in which water regulated the pressure and differed from the one used by Calcar. The diph-

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(1) Berl. klin. Woch., Sept. 26, 1904.
(2) Ibid., Feb. 20, 1905.

theria toxin used had a strength of 0.001 c.c. to kill a 250 gm. guinea-pig. He found that about 30 per cent of the toxin dialized without pressure. When dialized with 10 c.c. water pressure for 24 hours, the toxin which had passed through showed a killing strength of 0.006 c.c. for a 250 gm. guinea-pig. In testing the neutralizing value of the toxin within and without, it was found this was the same. If the dialization was allowed to continue for several days longer the results were also the same.

The writer thinks Calcar's fluids must have become infected to show the results reported. He further doubts the latter's experience in working with toxins. He concludes both toxin and toxon pass through the dializer at the same time. In Calcar's work it is further not proven that the dialized fluid causing paralysis contained no toxin by injecting larger doses than were reported. Roemer's figures give .0063 as a fatal dose for a 250 gm. guinea-pig, while .006 cause paralysis in a 330 gm. guinea-pig in the course of four weeks.

Boldireff[1] *experimented upon himself* with diphtheria toxins. He injected from .0001 to .8 c.c. toxins in the cellular tissue for a period of 36 days. At the end of this time, tests for immunity showed that his blood had a value of .4 of a Behring unit per c.c. No bad results were noticed, and in fact he increased some in weight. It would seem clear that even small doses of toxin repeated very soon give rise to a protective immunity. Similar experiments made by the writer on animals showed that they were well protected from infection by the bacillus.

Krasnoff[2] writes regarding the effect of *diphtheria toxin on the heart and respiration:* Paralysis of the vaso-motor centers in the medulla and of Goltz's center takes place, while the peripheral vaso-motor centers remain intact. The paralysis of these centers causes a progressive decline in the blood pressure, beginning at the height of the intoxication. The rhythm of the heart follows the altered condition, but its excitability and activity is retained. The controlling apparatus of the heart is influenced first, leading to increased excitability and later to paralysis of the

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(1) Rousskii Vratch. II, No. 39.
(2) Medizinískoe Obozryenie, 1904, No. 20.

vagus. With paralysis of the vaso-motors there also occurs a fall in temperature. Death is due to paralysis of respiration.

By *circulating diphtheria toxin through the veins of fresh livers,* Lauder Brunton and Bokenham[1] showed that the lethal dose is greatly diminished. It does not matter whether blood or some indifferent fluid is used for the purpose of circulation. The bile and the juices from such livers have a slight antitoxic effect. They consider that these experiments show the physiologic action of the liver on albumin and peptones has its analogue in its effect in reducing the poisonous properties of toxic bacterial proteids.

Pick and Schwoner[2] assert that more attention should be directed towards the *composition of antitoxin.* Apparently it is assumed that antitoxin is fairly constant, and the variations of toxin are determined by experiments. Their experiments were conducted with one given toxin towards different immune sera. It was found that with some sera fractional saturation would be in direct proportion to the amount of toxin used, so that the result might be represented by a straight, gradually ascending line. With other sera this was not the case, it being more complete with certain fractional parts than the amount would warrant. This, represented graphically, gives a curved line. The variability is due to the properties of the immune sera, and not to the *toxins.*

Vincent's Angina. Crandall[3] reports a case of this rare infection of the throat and mouth. The clinical history is submitted at length. The chief point is in the long continued ulceration and in the formation of purulent pseudomembranes. Bacteriology of the condition: Cultures made on ordinary media did not prove successful. Direct microscopic examination showed Spirochaete denticum and Vincent's[4] bacillus in great abundance. The slides showed the organisms intimately mixed and having relatively few saprophytes present. Specimens taken from the edge of

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(1) Jour. of Path. and Bact., November, 1904.
(2) Zeits. f. Expt. Path. u. Therap., 1905, Helf 1.
(3) Jour. Amer. Med. Assoc., July 3, 1904.
(4) Annales de l'Institut Pasteur, 1896.

the gums showed them also present, but with increased number of saprophytes. The organism stained well with ordinary stains. The bacilli were fusiform and rather large—8 to 12 *m.*—while the spirilla were 36 to 40 *m.* in length. With active treatment the number of organisms rapidly disappeared.

Dysentery Bacilli. Duval[1] deals with the isolation and study of another member of this interesting group. The specimens were taken from the gut and contents of a fatal case of dysentery. The method consisted in making suspensions of the scrapings from the intestinal mucosa and the blood-stained mucus in sterile saline solution. The tubes were shaken and allowed to settle. From the supernatant bacterially cloudy fluid a series of 24 agar plates was made. One loop of the fluid was used for each plate. In the agar used the omission of beef-extract makes it more clear, and the colonies can be more readily differentiated. In 24 hours dull pearl gray colonies appear beside the colon colonies, which are more dense and glistening. These pearl colonies are transferred to the semi-solid medium of Hiss by stab inoculation and incubated for a further 24 hours. In this medium *B. coli* causes rapid gas production, while *B. typhi* causes even clouding of the medium. B. dysenteriæ remains along the needle tract, not showing cloudiness, and does not ferment. Cultures conforming to this were studied further, especially by agglutination tests.

The bacillus isolated from this case had a morphology like B. dysenteriæ, being 1 to 3 *m.* in length, rounded ends, singly and in pairs, non-motile, and staining somewhat uncertainly with methyl blue, while Gram's method is negative. The organism grew like B. dysenteriæ, with the exception that in neutral litmus milk it at first induces acidity like the type organism, but after 48 hours the milk returns to the blue color; several days later it becomes acid and remains so. There is no coagulation. It was found that the bacillus fermented lactose with considerable rapidity. This property, with the second acid development in litmus milk, makes it different from other dysenteric

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(1) Jour. Amer. Med. Assoc., Aug. 6, 1904.

bacilli. Agglutination tests showed that it was positive with the patient's blood 1:400 dilution. Other bacilli tried showed Flexner-Harris' culture 1:200 dilution; Shiga negative; B. typhosus positive 1:80 dilution and paratyphoids negative. Cultures of the author's bacillus were likewise agglutinated by blood from other typhoid cases.

Tayler-Jones[1] reports her results of the *bacteriologic examination of cases of dysentery* occurring in Washington, D. C., as regards the presence of B. dysenteriæ (Shiga). During the summer of 1903, when this investigation was made, the writer found dysentery was rare in Washington. Twenty suspicious cases were examined; of these 6 gave positive results for B. dysenteriæ, 6 were negative bacteriologically, but suggestive clinically, while 8 were negative both bacteriologically and clinically. Flexner's method was used. The transfer to bouillon was usually done at the hospital or home, and taken to the laboratory for plating. In the positive group the number of colonies of dysentery bacilli isolated ranged from 1 to 40.

The conclusions reached are that Washington, D. C., is to be included in the geographical distribution of B. dysenteriæ. The Shiga bacillus was found both in children and adults suffering from dysentery. The alkaline (Shiga) and the acid (Flexner) types are found both in children and adults. An alkaline-type bacillus isolated from 1 case showed a variation from the type in that it produced some gas in glucose agar not previously sugar free, but no gas when it had been freed from sugar. None of the other Shiga bacilli fermented in this medium.

Morgenroth[2] reports the findings on microscopic and cultural examination of cases of *dysentery in China.* Amebæ were not found as abundantly as might be expected; being absent in some cases in which there were liver abscesses. He noted cells much like amebæ in these abscesses, but nonmotile no doubt being dead. The pus was often found sterile. In most cases the bacteria isolated from the pus or from the wall of the abscess were staphylococci or streptococci. When such pus was in-

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(1) Jour. Amer. Med. Assoc., July 2, 1904.
(2) Archiv fuer Schiff und Tropen-Hygiene, VIII, Heft 1.

jected into animals it did not cause abscesses, but the animals would die of septicemia. Bacilli resembling B. coli were isolated and these showed the peculiarity of agglutinating when tested with the patient's blood, but not with the blood of other persons. The B. dysenteriæ and several of its varieties were isolated. Some of these only agglutinated with the patient's blood from whom they had been obtained.

An *epidemic of dysentery* at Lyons, France, was studied bacteriologically by Braun, Roussel and Job[1] and the specific organism isolated. For purposes of isolation the Drigalski-lactose-nutrose-agar was used. The organism isolated was of the dysentery group and the cultural findings are described. Antidysenteric serum was used for specific differentiation. The organisms isolated from the different patients all reacted with serum taken from the cases involved in the epidemic; 67 cases of dysentery occurred.

Weaver and Tunnicliff[2] *made cultures from 102 cases of infantile diarrhea* with the view of isolating dysentery bacilli. From 26 cases (25.4 per cent) cultures were obtained which corresponded to the types of dysentery bacilli. Eleven cases corresponded to the Flexner-Harris type, and 17 to the bacillus Y-type; 2 other types were isolated. None corresponding to the Shiga type were isolated. A limited number of tests were made to determine the relations of serum reactions with such bacilli and dysentery bacilli to the cases in hand. It was found the serum from scarlet fever, measles and typhoid agglutinated the bacilli about as well as that from the patients. It would seem that the agglutinating power of the patient's serum is no aid in identification of the bacilli. In view of the finding of dysentery group bacilli in normal milk stools and small numbers in summer diarrhea it is not safe to say that they are the causal factor in most summer diarrheas.

Gonococcus Infection. Cases of general gonorrheal infection are becoming more and more in evidence. Busquet and Bicheloune[3] discuss this subject. In their case the

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(1) Lyon Medical, Jan. 1, 1905.
(2) Trans-Chicago Path. Soc., Nov. 14, 1904.
(3) Rev. de Méd., May 10, 1904.

presence of abscesses containing gonococci in pure culture is of chief interest. A man had an injury to his leg some 20 days previous to contracting gonorrhea. In a week there was pain and swelling, and an abscess was diagnosed. This contained pus and blood and on microscopic examination the *Gonococcus.* About this time a similar abscess developed on the forearm. Cultures of this pus on ordinary media remained without growth, but on a medium consisting of 20 c.c. gelatin and 5 c.c. pleuritic fluid a pure culture of the Gonococcus was obtained. The rarity of such abscesses is noteworthy, especially because direct subcutaneous inoculation of cultures have been negative.

Bacteriology of Rheumatism. Beattie[1] describes the organism previously reported and studied by him. Microscopic and staining characters: Small micrococci in pairs or short chains either when seen in the tissues or in cultures. In milk bouillon, chain formation is more pronounced, but not exceeding a dozen elements. Some of the individuals are oval in outline; capsules are absent. Degeneration forms are common in older cultures, the cells being swollen and somewhat elongated. Stains well with ordinary stains and is ositive to Gram's method.

Cultural Characters.—Media neutralized to +10 degrees.

Bouillon—In twenty-four hours at 98.6° F. there was slight clouding, later clearing with a slight flocculent deposit. The media became decidedly acid. There was no indol.

Glycerin bouillon—The growth was very slight and the fluid became clear in a few days. A distinct deposit formed. Alkalinity was somewhat diminished, but did not become acid even after three weeks.

Peptone solution—Appearance much as in bouillon, but acidity was more marked.

Gelatin stab—In two days minute colonies appear along the needle track—no extension on surface and no liquefaction or gas production.

Gelatin streak—Small whitish colonies develop along the streak, but do not extend or fuse to any extent.

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(1) Brit. Med. Jour., Dec. 3, 1904.

Gelatin plates—The colonies are small, round and distinctly granular. The edges are regular.

Agar streak—Small transparent colonies slightly raised and not spreading. More growth at 68° F. than at 98.6° F.

Deep agar—No growth.

Blood agar—(This is the best medium.) Small whitish raised colonies appear which later show some tendency towards fusion. The red blood pigment gradually charged to a rusty brown or chocolate color. Cultures remained alive a long time on this medium.

Blood serum—On human serum there were small raised colonies that gradually coalesced and formed a uniform whitish streak.

Milk—In 24 hours no acidity or coagulation occurred. In three days acid and coagulation.

Milk alkaline to litmus—Similar results.

Milk and acid bouillon—Acid and coagulation.

Potato—No growth.

Anaerobic cultures—Deep glucose-agar, slight growth, no surface spreading. In format bouillon no growth developed.

Inoculation experiments. Intravenous injections caused endocarditis, polyarthritis and chorea. The polyarthritis usually develops in three days. Subcutaneous inoculations even in large doses did not cause suppuration—as has been reported by Paine and Poynton. It is important in this connection to be certain that the culture is pure before and after the inoculation experiment.

Experimental Transmission of Mediterranean Fever. Ross and Levick[1] present a preliminary notice of experiments. In view of the results obtained by the United States Yellow Fever Commission it was thought that possibly mosquitoes might have to do with the transmission of this disease. The first line of experiment was with fomites and by direct contact. Two cases were treated on board ships by non-immunes without a second case appearing. The attendants slept in the bed clothing of the

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(1) Brit. Med. Jour., April 1, 1905.

patients. The diagnosis in these cases was established by demonstration of *Micrococcus melitensis* in the blood.

The second experiment involved infection by inhalation of infected dust. The urine from a case of Malta fever and a culture of *M. melitensis* were dried and powdered. The dust was inhaled and swallowed but the disease was not contracted.

Third, infected water was employed. The urine from a pronounced and typical case of Malta fever was mixed with water in the proportion of 10 oz. of urine to 5 gallons water. A tumbler of this mixture was drunk by two non-immunes without effect.

The fourth experiment was with mosquitoes of the Culex, Stegomyia and Acartomyia varieties. These were allowed to draw blood from cases during the early stages and during the height of the disease, and were then transferred to susceptible persons several times, but these experiments, like the others, were complete failures.

The greatest care was used to avoid contact with cases, or to go into places where the disease was known to exist. The writers hope by continuing their experiments to determine the manner of transmission.

Meningococcus. Sorgente[1] discusses the relative merits of the different bacteria isolated from cases of cerebrospinal meningitis, and other diplococci. There are two type groups: *Jaeger-Heubner,* showing a mass arrangement with occasional chains, positive to Gram's method and showing an abundant growth on media. Growth also takes place at 64.4° F. in bouillon and on agar, gelatin and potato. *Group Weichselbaum:* Negative to Gram's method, upon agar small isolated drop-like colonies are formed, at room temperature no growth. The writer reviews 28 described cultures from the cerebro-spinal fluid and 8 from other sources. These were studied by serum reaction using the serum of experimentally immunized rabbits.

The conclusions are that it is not possible by agglutination experiments to distinguish between the types in question, consequently they must be considered as varieties of

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(1) Zentralb. f. Bakt., XXXIV, Heft 1.

the same species. The organisms isolated from cerebro-spinal fluid show a marked difference in their agglutination properties from those otherwise isolated. The serum of a patient with cerebro-spinal fever will agglutinate the meningococci isolated from himself in dilutions of 1:100 and meningococci from other cases in dilutions of 1:50, but will not cause reaction with diplococci from other sources. If an animal is immunized with an ordinary strain of diplococcus, the serum obtained is negative with meningococci.

The writer tested the antipneumococcus serum of Pane and states it is negative toward meningococci.

Pneumococci in Scarlet Fever. Ruediger[1] examined swabs from the throats of patients by the blood agar method for pneumococci and streptococci. The swabs were rinsed in 1.0 c.c sterile broth; the latter is immediately used to inoculate 6 to 8 blood agar tubes which are poured into plates. The blood agar is prepared by adding 8 to 10 drops of fresh defibrinated human or animal blood to melted agar tubes, containing 5 c.c. and cooled to 113° F. By making the plates at once the relative proportion of organisms present may be determined. The streptococci show as small grayish colonies surrounded by a clear zone where the corpuscles have "laked." Pneumococcus colonies are surrounded by an opaque area having a greenish tinge. The result of the examinations showed that pneumococci are abundant, sometimes in greater abundance than streptococci.

Pneumococci and Parotitis. Pennato[2] reports the results of cultivations from the fluid of parotitis during the course of lobar pneumonias. This condition occurs at times, and writers have been quite diverse as regards its significance. In this instance pneumococci were cultivated from the blood and from the inflamed parotids. There was no distinct suppuration. The possibility of direct infection of the gland through Steno's duct is considered, but no definite conclusion is presented.

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(1) Trans-Chicago Path. Soc., April 10, 1905.
(2) Rif. Med., June 1, 1904.

Streptococci. A. Hamilton[1] deals with the extent and danger of spreading streptococci by moist particles thrown into the air. The conclusions reached are: that streptococci are expelled from the mouth in invisible droplets caused by coughing, speaking, whispering, crying or forced breathing. They may be scattered for a distance of 14 inches. Of 50 scarlet fever patients, 33 were found to expel streptococci in this manner. Of 50 normal adults, 42 were found to expel streptococci by coughing or speaking. The streptococci thus disseminated may be inhaled by others, and thus give rise to streptococcic infections. They may also fall upon the surfaces of operation wounds.

It is possible that virulence may be modified by such a passage from person to person in the same manner as arises in cultural experiments or in animal inoculations. A case of simple scarlet fever may be converted into one of scarlatinal sepsis, and a surgical infection traced after all precautions have been followed. Cases of scarlet fever with streptococci in the throat should be isolated from other cases without such a complication.

The use of blood agar plates after Littman's method is reported of great value in *diagnosis of streptococcic infections in puerperal cases* by Fabre and Amstad.[2] Blood cultures are made and the lochia is similarly plated. The blood or lochia is mixed directly with melted agar to which a drop of fresh blood has been added. Petri plates are poured and after hardening are placed in the incubator. In the course of 24 hours colonies will appear and the streptococcus colonies are marked by being encircled by a clear area where the corpuscles have "laked" and the hemoglobin has been appropriated. In some reported cases the lochia showed streptococci, but they were absent in the blood.

Ruediger[3] concludes his results are corroborative of most previous workers in the field of *streptococcus infection*. He found that leucocytic exudate, the cell free exudate and suspensions of leucocytes or suspensions of bone marrow in serum or defibrinated blood would kill non-virulent strep-

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(1) Jour. Amer. Med. Assoc., April 8, 1905.
(2) Lyon Médical, April 16, 1905.
(3) Jour. Amer. Med. Assoc., Jan. 21, 1905.

tococci, but not virulent cultures. Suspensions of organ cells do not kill streptococci. Leucocytes in the animal body take up living streptococci.

Considering all facts, it would seem that the leucocytes and bone marrow are the most important factors in combating streptococci in rabbits and guinea-pigs. That the leucocytes take up living streptococci in the animal body and probably destroy them was shown by the writer, but the cell free exudates also destroy them, thus indicating an extra- and an intracellular destruction of these bacteria. When virulent streptococci are grown in heated serum, they secrete a substance which is toxic for leucocytes. This may explain why virulent streptococci are not taken up by phagocytes. If we accept the view that the leucocyte is the principal agent of defense against streptococci, the practical importance of the formation of such a toxin is apparent, because by its action the defense on the part of the host is greatly depressed or entirely destroyed.

Kerner[1] studied 16 virulent and 7 non-virulent strains of streptococci from various sources as regards their *hemolytic and agglutinating properties.* Eleven virulent cultures showed hemolytic power; of the non-virulent strains, 2 showed distinct hemolytic activity. The amount of relative laking may be noted by observing the degree of red color in the test tubes. Agar plates to which blood was added show a clear ring about the colonies due to local laking of corpuscles. The extent of this laked area cannot be considered as of value in relation to quantitative determinations.

Streptococcus cultures that have just been isolated from animals show strong hemolytic powers. When they are cultivated artificially, especially in sugar bouillon, this gradually decreases. If bouillon cultures are maintained at room temperature their properties remain fairly constant for 7 to 14 days. The addition of 2 per cent salt to the bouillon restrains the hemolytic activity. When heated for 30 minutes at 131° F. all hemolytic power is lost. The filtrates from bouillon cultures do not possess this power. When

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(1) Zentralb. f. Bakt., Abt. XXXVIII, Heft 3.

grown in liquid blood serum the filtrates obtained therefrom show a weak activity.

Agglutination properties are developed in the serum of animals which have received repeated small doses of the streptococcus in question. The strength of the serum is not indicated by the number of injections or the amount of cultures applied. The strength of the serum of animals continuously injected increases gradually for 2 to 4 months; it remains stationary for a period and gradually decreases even if the injections are continued. No agglutinating value was found with the urine of experiment animals. Only such streptococci as are highly pathogenic for man or animals show these properties in the higher degrees of activity.

In a discussion on the *clinical use of antistreptococcus serum* at the Berlin Medical Society,[1] Fritz Meyer stated he desired to present the subject, based on clinical and experimental observations as regards the indications and contra-indications. Is the status such that the serum should be used, or are there possible dangerous consequences? For clinical purposes only a high grade serum can be used—*i. e.,* there must be a sufficiency of immune bodies present, and, moreover, it is important that these should not be diluted. Prophylactic and therapeutic uses require special attention. As a prophylactic measure it can be used in angina, erysipelas, scarlatina and endometritis. In septic cases it is to be used therapeutically. In localized streptococcus infections it is to be used in the hope of limiting extension, especially to the blood. Animal experiments strongly indicate that such a protection is to be expected. During the first 12 to 20 hours after an injection the effect cannot be noted; in fact, during the first hour the clinical conditions may appear worse. Later a sedative influence is noted. Puerperal patients are able to sleep and the mucous surfaces become moist again.

The speaker lauded the serum for aborting severe anginas and in combination with diphtheria antitoxin in cases of septic diphtheria. In erysipelas the results have not been flattering, because in the first place the injected

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(1) Zentr. f. Bakt., XXXVI, Nos. 10-11.

serum reaches the streptococci in the lymph spaces only with difficulty and then the bacteriolysis that would occur might rather aggravate the condition by liberating toxins. In recurrent or wandering erysipelas it is advisable. An unusual number of blisters are often noticed after injections in erysipelas. The results in scarlet fever do not warrant any statement that the etiologic factor or course of the disease itself is modified. Desquamation does not occur earlier nor is its character in the least modified. The mixed or secondary infection with streptococci is, however, benefited and less albuminuria or secondary inflammation is seen. In puerperal fever it is advisable especially early because it is impossible to place a limit upon the ultimate extension of the infection. All cases showing fever in the puerperium should receive prophylactic injections. As contraindications, Meyer considers its use as dangerous in ulcerative endocarditis, inflammations of serous membranes, long-standing pyemic infections and for the mixed infections of tuberculosis.

Aronson said the antistreptococcus sera belong to the antibacterial sera, but differ from such as are antagonistic to typhoid and cholera, in that these dissolve the bacteria by the serum activity alone, while the cellular activity, in addition, always assists in disintegration of streptococci. Another difference in action is also seen in animal experiments. An animal inoculated with a fatal dose of typhoid bacilli cannot be saved even with a large dose of antiserum if given later than two hours after the injection. On the other hand, those injected with a fatal dose of streptococci may be saved even after 24 hours, when streptococci are circulating in the blood, by a dose of antistreptococcus serum.

The greatest difficulty is in the testing of sera, and especially because human streptococci are not uniformly pathogenic for animals. As regards the indications for the serum, he agreed with Meyer, but he does not recognize any contraindications.

Huebner reported having used the different sera on the market in scarlet fever cases, and found—contrary to the theoretic advantages—that the results were unsatisfactory, and has since discontinued its use.

In scarlet fever the streptococci are entirely secondary to the disease, as is now generally recognized, and the serum has no effect on the specific process. When given in cases of mixed infection, the fever was seen to rise again in 3 to 4 days, and sometimes the patients died later of sepsis. Recovery from large abscesses in scarlet fever under use of streptococcus serum cannot be attributed entirely to its use because at times there may be spontaneous cure. His results in diphtheria-mixed infections in combination with diphtheria antitoxin have not been sufficiently encouraging to warant its continuance.

Marmorek stated he had been experimenting with and using antistreptococcus sera since 1896. As many strains of streptococci as possible must be used in immunizing the horses, and the serum for therapeutic purposes must not be taken by bleeding earlier than 6 to 7 weeks after the final injection of streptococcus. If the animals are bled earlier than this the blood will contain toxic bodies. These may be the cause of the bad results seen at times clinically. With his own serum he had never seen an untoward result, and consequently knew of no contraindication for its use. As regards dosage the limits can be placed between 30 c.c. and 50 c.c. for the case. Amounts of 250 c.c., as suggested by Moser, are not countenanced by him.

Wolff called especial attention to the statistics and reports of antistreptococcus sera used in cases of puerperal fever. The indications for its use here should depend upon the finding of streptococci in the lochial fluid or in the patient's blood. In many instances other organisms are the cause of the infection, and the unsatisfactory results therefore obtained give a wrong impression as to the value of these sera.

Beitzke added that the mixed infections of puerperal and scarlet fever must always be taken into account. In his experience antistreptococcic sera were worthless in combating staphylococcus infection.

Bumm reported that the beneficial results of using these sera are always an amelioration of the general symptoms. Local tissue changes and suppuration are not benefited by their use.

Hemboldt used sera as a prophylactic measure in 20 obstetric operations, with good results.

In closing, Meyer remarked that producers of sera generally waited 6 to 7 weeks before bleeding the animals. Aronson's serum seemed to him specific only for certain very virulent streptococci, and in some instances increased temperature was observed after its use.

Bergey[1] presents experiments regarding the *identity of streptococci from cow's milk and the specificity of anti-streptococcus sera.* Goats and rabbits were injected with streptococci from cows, for some time, and the agglutinating and protective properties of their sera towards streptococci determined. The agglutination tests showed it was present in the sera of these animals, and that positive reactions could be obtained with the strain used in immunizing the animal, and also with strains from other sources. The end reactions were with about the same dilution. These results would confirm other observations that streptococci from various sources are closely related.

White mice were used to test the protective value of the sera. A mouse received 1 c.c. of serum in the peritoneal cavity, and 24 hours later a fatal dose of streptococci, also intraperitoneally. The results did not indicate any active protective influence; however, in some instances the life of the animal was considerably prolonged. The sera obtained by Bergey were apparently of the same strength as a sample of Aronson's serum used at the same time. Test-tube experiments were also made to show the presence of bactericidal properties. The results of these were uniformly negative. The addition of leucocytes showed that large numbers of streptococci would be taken up *in vitro,* and would account for the disappearance of streptococci under these circumstances.

The influence of non-fatal doses as regards protection against later fatal doses was tried, but with very irregular results. It general it may be said that these repeated non-fatal doses do not confer immunity. In some instances an apparent toleration was established, but in others a cachetic condition developed, in which the animals would succumb

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(1) Jour. Amer. Med. Assoc., July 23, 1904.

to a smaller dose than usual. He confirms the observations of Schenck, who found soluble toxins in streptococcus cultures. Bergey's toxin required a dosage of 2 c.c. to kill mice. He concludes with others that the toxins alone do not cause all damage from streptococci. By using this toxin a mild immunity and antitoxic serum was obtained. As regards the mechanism of protection against streptococci, it is mostly due to stimulation of phagocytosis.

Streptococci and Puerperal Fever. Baum and Sigwart[1] examined the vaginal secretion of 103 women in the last months of pregnancy, and found streptococci in 38.16 per cent of those examined once; in 83 per cent of those examined twice, and in 55 per cent of 9 multiparæ. Of those showing streptococci, some 20 per cent developed fever, while 11 per cent of negative cases later showed fever. In 75 per cent of all women examined aerobic chain cocci were found.

Staphylomycosis. Berezegovsky[2] reported the case of a young girl of 10, who died in a few days from an apparent osteomyelitis. Pure cultures of Staphylococcus aureus were obtained from all the tissues, exudates and organs. Operations upon the infected bones will not save these patients, and the general mortality is very high.

Spirillum Pyogenes Mezincescu. Doerr[3] describes a spirillum which he thinks identical with one described by Mezincescu[4] from a case of extensive suppuration of serous membranes. Smears made from the pericardial and pleuritic pus show thin comma-shaped organisms 1 to 2 *m.* in length, and at times longer, grouping with 2 to 3 turns in the spirals. Here and there one may be included within a leucocyte. An injection of 2 c.c. of pus into the peritoneal cavities of white mice caused death of the animals in 48 hours. Large numbers of spirilla were found on making smears from the peritoneum. The only satisfactory cultures were in bouillon, and these developed slowly.

The only growths obtained from the bouillon were on

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(1) Beitr. z. Geb. u. Gyn., XVII, No. 8.
(2) Medicinskoe Obozryenie, 1905, No. 1.
(3) Zentr. f. Bakt., XXXVIII, Heft 1.
(4) Ibid., Bd. XXXV, H. 2.

human serum-agar. The colonies were fine, and much like influenza. In bouillon it was possible to keep the growth alive for a considerable number of generations, but on the serum-agar medium it died out rapidly. Motility was absent in all specimens. Other laboratory animals were not infected after being injected. The writer suggests that if this is not the cause of the suppurative pleuritis and pericarditis, the original organism must have died while these spirilla invaded as saprophyte.

Typhoid in Well Water. The finding of typhoid bacilli in water is not frequently reported; however, Stroeszner[1] records a successful result. The water in question was badly contaminated and the presence of the bacilli was presumed. The method used was that of Hoffman and Kicher.[2] To 900 c.c. of the suspected water is added a solution of 10 grams nutrose in 80 c.c. of distilled water; one of 5 grams caffein in 20 c.c. of water, and another of 0.1 gram crystal-violet in 100 c.c. of water. The mixture is incubated for 12 to 13 hours. Plate cultures were now made on Drigalski-Conradi medium. Colonies that appeared bluish and moist were transplanted to bouillon, from which the series of subcultures was made for identification. Finally the serum test was made with each culture.

Typhoid in Earth. Ruelmann[3] found that when typhoid bacilli were added to earth in flasks it was possible to recover them after 18 months, even when the earth had dried to powder. (The earth used in these experiments was sterilized.) The only noticeable change in the biologic character of the cultures was in the agglutination value of the bacillus being reduced to 1:2500 in place of the original 1:10,000-40,000 dilution. Slight irregularities noted in the first culture isolated disappeared in the subcultures after plating several times.

Some comparative tests of *newer methods for isolation of B. typhosus from the feces* are reported by Reischauer.[4] These are the v. Drigalski-Conradi medium; Lactose-lacmoid-nutrose-agar; Endo, the same, but containing fuchsin

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(1) Zentr. f. Bakt., XXXVIII, H. 1.
(2) Hygienische Rundschau, XIV, No. 1.
(3) Zentralb. f. Bakt., XXXVIII, Heft 4.
(4) Ibid., XXXIV, Heft 1.

solution as indicator (Kicher and Hoffmann); caffein added to various media (Loeffler); malachite green solution in media (Windelbandt); addition of immune typhoid serum to the suspected mixtures, and that of Cambier, allowing the more motile typhoid bacilli to grow through a filter and expecting them to be in almost pure culture on the opposite side.

He finds the Kicher-Hoffmann method is of relative value only as it restrains intestinal bacteria but it does not insure a growth of typhoid such as is claimed. The same may be said of the addition of caffein to the Drigalski medium. For general purposes the simple use of the Drigalski plate method, or the Endo's modification, proved most satisfactory. All of the methods using sera and restraining agents on large quantities of feces were found unsatisfactory, because of the tendency of some organisms to overgrow in the medium. Experiments with water samples gave results similar to those made with maceration and dilution of feces specimens.

Monti[1] has been testing the Drigalski-Conradi method for *isolation of typhoid bacilli from the stools,* and finds he cannot place the same reliance on it as stated by several workers. Negative results do not exclude the presence of typhoid bacilli. He considers it valuable in conjunction with others as an additional control.

Marschall[2] finds the *method of Endo* rapid and cheap. The differentiation of B. coli from the typhoid-paratyphoid group is distinctive, as the colonies of the former are red and the latter colorless. This is an advantage over the Drigalski medium, especially when work has to be done by artificial light. The restraining action upon the other intestinal bacteria is more marked with this modification. Subtitis and Proteus colonies can be easily distinguished on the plates from those of typhoid and colon bacilli.

Automatic Mixer for the Widal Reaction. Paltauf has called attention to the necessity of exactitude in performing serum reactions. The ordinary methods of meas-

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(1) Archivio per le Scienze Medische, 1905, Nos. 1 and 2.
(2) Zentralb. f. Bakt., XXXVIII, Heft 3.

uring quantities of serum, culture, etc., are far from exact.

Pfaundler's suggestion of using the white pipette of the Thoma-Zeiss haemocytometer was an improvement but somewhat troublesome.

Pfaundler[1] describes an instrument which he has originated for the rapid and accurate measurement of quantities for serum reactions.

The apparatus consists of a glass stop-cock rotating in a hub from which four glass tubes rotate. The stopcock has a cavity in its barrel of 0.4 cc. capacity which by rotation may be made to communicate with any of the glass tubes.

By means of this cavity a definite quantity of fluid can be transferred from one tube to another.

Technic for Widal Reaction. There have been many methods advised for collecting blood for the Widal reaction. While the ordinary method of collecting the blood on a cover glass, a piece of mica paper is very convenient it is far from accurate.

It is known that icteric serum and the serum of patients infected with other members of the colon group agglutinate the typhoid bacilli. Further it is known that the specificity of the reaction is the more probable the greater the dilution above 1:100. Thus the chances for error in the ordinary methods of obtaining serum is recognized.

Schottelius[2] advises the use of a centrifuge tube containing a cotton swab on a wire one end of which is imbedded in the rubber cork of the tube. The method is as follows: 10—15 drops of blood is absorbed by the cotton swab which is then replaced in the tube; after the blood has coagulated the tube is centrifuged and from the serum thus obtained a definite quantity is removed with a graduated pipette.

The experiments of Joergensen[3] on variations in agglutinins during typhoid infection show, that, for the purpose of quantitative determination of agglutinin value, the

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(1) Müench. med. Woch., No. 7, 1905.
(2) Ibid., No. 15, 1905.
(3) Zentralb. f. Bakt., XXXVIII, Heft 6.

microscopic test is to be preferred. (The writer, however, admits a possible 9 per cent of failure.) Following an injection of typhoid bacilli in rabbits or goats the agglutination value of the serum will be found in three phases: (1) 2 to 3 days before any agglutinin is found—latent period; (2) 5 to 9 days, a gradually increasing period of value, reaching its maximum on the 7th to 9th day; (3) a fall appearing suddenly and then gradually followed by a more or less gradual decline. Daily injections of small amounts of culture are followed by the same curve-result, but the first and second phases are longer, and the third appears as abrupt as usual, but remains low, even if the injections are continued. When a second injection of the culture in question, or some other, as B. coli, is made during the second phase, the resulting increase in agglutinins produced is relatively slight. The blood of typhoid patients shows an agglutination curve corresponding more to that caused experimentally by the injection of small doses repeated daily.

The differentiation of strains of typhoid bacilli and paratyphoid organisms by serum tests has been reported by a considerable number of observers. Recently Falta and Noeggerath[1] report such a series of tests with *practical bearing on the diagnosis of typhoid fever by Widal tests.* In those cases where the reaction does not appear or is very much delayed, it is probable that the culture used in making the tests is one only relatively agglutinable toward the serum of the causal organism. Such unsatisfactory results can be avoided by testing the patient's serum with several organisms of different strains. This is of most importance early in the case: because later, when the serum is more active, the general evidence of reaction is usually plain. The presence of antiagglutinins is also a possibility. These occur at times in the blood of healthy persons and animals. The writers do not think this effect on cultures is due to the proagglutinoids of Eisenberg, but rather to an altered thermolabile agglutinin. When somewhat dense bouillon cultures are used it is possible to avoid an irregular result.

By numerous carefully prepared charts of typhoid fever patients, Iversen[1] shows the *changes in agglutination* of the patient's sera during the course of the sickness. The curves of agglutination strength show much variation, and it is only in a few general particulars that they coincide. In mild uncomplicated cases the value of the serum rises slowly (to 1:100 to 1:500 dilution). At the end of fever or beginning convalescence there is a sudden rise in value, and as sudden a fall (1:1000 to 1:5000 dilution), and when this lower value is again reached it may persist for a long time without special variations. In case of recurrence of the disease, the agglutination strength is always higher during the recurrence than during the original infection. Sometimes the reaction is absent during the first attack, but appears marked during the second. Sometimes the property disappears during the convalescent period, while in other cases it persists for years to a limited degree. In severe cases and in those in which there is a fatal termination in 3 or 4 weeks, the serum shows an increasing value up to the time of death. Cases of walking and atypical typhoid usually show a low and irregular agglutination value in their serum. Very severe and complicated cases give a curve of value showing irregularity, and with frequent rises and falls. When cases are complicated with diplo- and streptococcus pneumonias there is a tendency for the serum activity to be depressed; at least the usual rise is prevented. Ten years after an attack of typhoid the writer reports the agglutination value of a person's serum to be positive in 1:100 dilution.

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(1) Deut. Arch. f. klin. Med., May, 1905.

A number of cases are described in detail with post-mortem findings, and records of Widal reactions where death was due to tuberculosis, septic diphtheria and jaundice, in which the serum value for typhoid was 1:150 to 1:250 dilution. In these there was no typhoid present or past. Owing to the fact that a positive Widal appears sooner or later during an attack of typhoid, it is a specific test and a cardinal symptom, but it cannot be considered as pathognomonic, because it occasionally is present in other conditions. As regards prognostic importance, it seems to have no bearing. There is no relation between the severity of

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(1) Zeits. f. Hygiene, Bd. L, Heft 1.

the attack or the height or duration of the fever. It is a biologic means of differentiation, but as to its entire significance, more information than that derived from clinical study must be had.

In 50 cases of icterus or liver affections Kaemmerer[1] *tested the blood for Widal reaction.* In 94 per cent it was negative. In 1 the result was positive in dilutions of 1 to 75, and in 2 others at 1 to 40. Apparently little effort to exclude previous typhoid was made by the investigator.

Freezing as an addition to serum technic for diagnosis has been studied by Borelli.[2] This consists in having an emulsion of typhoid bacilli in a test tube, and adding to it the serum or blood, often dried on filter paper and dissolved. The tube is now placed in a freezing mixture and frozen. When it thaws the agglutinated clumps can be seen. The method is specific, but not quite as delicate as the usual Widal test. The entire procedure is simple and fairly rapid. Besides being a macroscopic test, it may also be microscopic where the clumped bacilli can be seen.

Sehrwald[3] finds that the cultivation of typhoid bacilli on potato or on media containing potato juice increases their agglutinability. By use of such cultures a strain of low value may be made to have a relatively high value towards specific sera, even after a short period of cultivation.

Kolli[4] comments on the *immunization of persons, especially soldiers, against typhoid.* The immunizing material is the dead culture of B. typhosus. This is prepared by inoculating slant agar tubes, and, after 24 hours' growth, mixing equal amounts of the bacteria mass scraped from the agar surface with physiologic salt solution. It is then carefully heated to 140° F. and preserved with 0.3 per cent phenol. It is filled into brown glass bottles, and sealed. In regard to its practical use on soldiers, it has been shown that these prophylactic injections are without danger, and are certain in protection. It is to-day more a matter of application than of principle. The procedures of inocula-

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(1) Berl. klin. Woch., XLI, No. 26.
(2) Reforma Medica, XX, No. 48.
(3) Deut. med. Woch., Feb. 16, 1905.
(4) Ibid., 1905, No. 12.

tion are practical and the resulting reaction is such that it can be recognized as being satisfactory or not.

So far the method has proved scientific and has been sufficiently controlled to prove its merits. Some points in regard to the dosage deserve special attention. The results so far noted in man are corroborated by previous observations on animals. This plainly indicates that the application of as large a dose as possible of the dead cultures results in the most lasting immunity. Repeated injections increase and lengthen the duration of the immunity. The succeeding and increasing injections have given better results than one or two. The amounts applied are equivalent to 1, 2 and 3 platinum loopfuls, and the time between injections should be from 8 to 10 days. During the first few days after an injection there is a stage of negative immunity, or decrease in bactericidal activity of the person's blood. During this phase it is very important not to allow the person under treatment to become infected with living typhoid bacilli. The use of small doses of the dead virus is unsatisfactory, because the resulting reaction may be too slight or may not occur at all. Moreover, it is not sufficiently characteristic to prove that the desired effect is taking place in the person. From observations to date it is not settled how lasting the immunity given by the injections will be, but it is not supposed that it is persistent for more than several years. So far 2,000 officers and men in South Africa have been immunized with excellent results.

Because of the presence of typhoid in South Africa the extensive use of *antityphoid inoculation of soldiers* has been tried. Musehold and Stendel[1] report the results in 634 men inoculated out of a detachment of 1,050 who were sent out in January. The inoculations were made midway between the clavicle and nipple. Radiating pains and some local swelling were present in most cases. Six per cent of the men inoculated remained in bed the next day. In 15 per cent there was vomiting; in most cases there was malaise, chilliness and twitchings of the limbs about 5 hours after the inoculations. In a few cases the neighboring glands became swollen and painful. It is stated that

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(1) Veroeffentl aus dem Gebiete des Militaer-Sanitaelswesens, 1905, Heft 28.

2 mg. of the dead culture of B. typhosus should be the highest dose for the first inoculation.

Flemming also reports the results obtained by repeating the inoculations with increased doses. A second dose of twice the amount gave in most cases a milder reaction. In 21 out of 93 a higher temperature resulted after the second injection. Twenty-four persons were injected a third time with a triple original dosage, and showed an even milder effect than that following the second injection.

Kuhn and Eggert also report the effects of injection in South Africa. Among 84 whites and 46 colored inoculated no serious results were seen. Thirteen who had had typhoid some years before did not react, while a number recently infected showed a slight reaction. The directions for application are essentially that 3 injections be made ten days apart; the dose to be .25 c.c. of the mixture presented for the first, and .6 and 1.5 c.c. for the other two treatments.

Typhoid Vaccine. Bassenge and Mayer[1] prepare a *typhoid vaccine* by agitating typhoid bacilli in distilled water for a long time. A yellowish fluid is the result; this is toxic, and a dosage can be determined by animal experiments. The writers give 2 c.c. as a vaccination dose, and state that the antibactericidal properties of the person's blood can be demonstrated even after a number of months.

The article by Stokes and Fulton[2] deals with the preparation of an *antityphoid serum and the results* in the treatment of 23 cases of typhoid, of which 2 died. The experiments date back to 1900, and have been in part previously published. Cultures of typhoid bacilli from different sources were used for the different animals immunized. In the main the cultures were pathogenic for guinea-pigs by injecting 1 c.c. intraperitoneally.

Well-grown hogs were immunized by injections ranging in amount from 10 to 1,000 c.c. at a dose at intervals of about 10 days. In 1 case the hog died of a typhoid bacteriemia with local necrosis. Most of the animals showed no special temperature change or other derangement. About

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(1) Deut. med. Woch., May 4, 1904.
(2) Jour. Amer. Med. Assoc., May 13, 1905.

two weeks after a final injection blood was drawn and the serum collected. The agglutination value of the hog serum rose from 1:100 dilution to 1:20-30,000 at the end of the immunization period.

Animal experiments previously described showed these sera had a protective influence when injected in amounts of 1-600 to 1-800 of body weight against 4 times the fatal dose in guinea-pigs. A slight antitoxic value was also present, as shown by the protective and neutralizing effect on dead typhoid cultures. The serum was given in 20 c.c. doses once or twice daily for a number of days. The results indicate some modification of the temperature curve, but

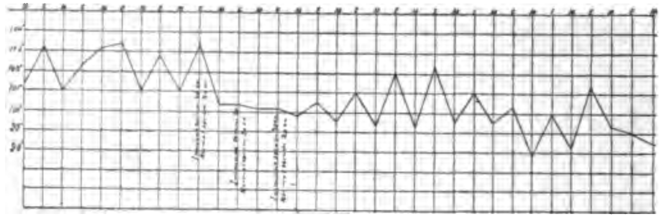

Chart 10.

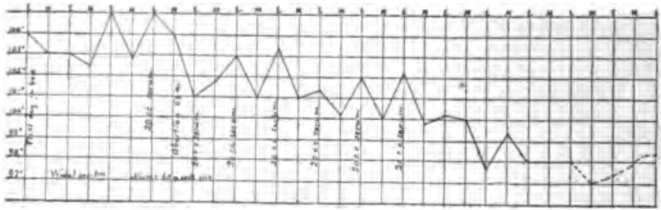

Chart 11.

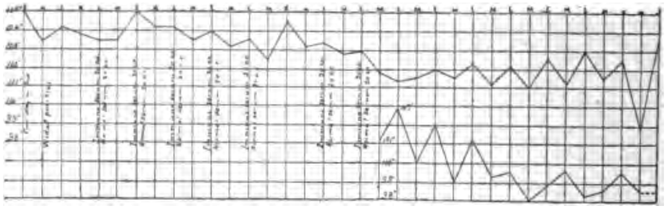

Fig. 15.

Results of treatment of patients with antityphoid serum of Stokes & Fulton.

no very marked influence, except in a few instances. The writers consider the effect in 15 to be decidedly beneficial.

Einhorn[1] reports on the *use of Jez's antityphoid extract in typhoid fever.* The serum was given subcutaneously in doses of 6 to 12 c.c., was begun as soon as the diagnosis was made, and continued until the fever had ended. As far as the results indicate, the writer could not see that the length of the sickness was decreased. He thinks, however, that the fever was influenced by longer remissions, and that the nervous symptoms disappeared owing to its use. The condition of the heart and circulation was excellent in every case, through that portion of the attack in which the serum was used. No particularly bad effects of the injections were noticed, although erythema occurred in several of his patients.

Chantemesse[2] reports very *satisfactory results in the treatment of typhoid with the serum* he has been making since 1897. This is prepared by injecting horses with soluble typhoid toxins. It is unlike antidiphtheritic serum in that it is only partly antitoxic, and requires assistance on the part of the patient to produce its good effect. The manner of use differs from antitoxin treatment because the dose must be reduced in amount in proportion to the severity of the case. But, as in other serum therapy, a much better result is to be expected when the injections are begun early. Other treatment is to be used as indications arise.

As to the results, the writer reports that no case of perforation occurred where the treatment was commenced before the 7th day of the fever. In cases begun later it seemed impossible to prevent perforation by its use, nor did other complications seem to be prevented. The total mortality reported from 1897 to date, under this serum treatment, is 4 per cent. General typhoid mortality in about the same district, and principally Paris hospitals, gave an average of 18 per cent. Perforation occurred in 1.6 per cent of the cases treated, which may be compared with 2.6 per cent of perforations in compiled statistics of typhoid.

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(1) Zeit. f. Diaet. und Phys. Ther., October, 1904.
(2) Presse Médicale, 1904, No. 86.

B. Coli. Experiments made by Padoa[1] go to show that the protective action of the liver against the toxins of B. coli is very marked. Naturally, the liver drains an area where infections are very possible, and yet primary infections of the liver are rare. The liver may show swelling, but is never affected to the extent seen in the spleen and kidneys. Padoa's method to show this protective power consisted in making injections of the same material into the portal veins of one rabbit and into the jugular veins of another, the toxic results being compared. Changes in the kidneys of these rabbits were noted especially. Three strains of colon bacilli were used, but the results were found to be practically the same. When injected the rabbits showed signs of prostration in 2 to 3 hours when the jugular was used, and 6 hours or longer in the portal vein. Diarrhea appeared, later convulsions and a marked cachexia. Forty rabbits were used. The results as regards death were as follows: In one experiment both recovered; in two, the 2 animals died at practically the same time; in one of these the portal vein animal lived three hours longer than the other, and in 17 experiments the portal vein-injected rabbit lived at least 24 hours longer than the other. In 5 experiments the animals with portal injections recovered.

The results show the protective influence of the liver as regards these toxins. In most of the animals degenerative changes in the kidneys and to a less degree in the liver were found. In a few instances increase in connective tissue was found.

A comparative study of the kidney changes showed they were more diffuse and more intense in the cases of jugular injection. The nephritic changes were mainly in the cortical zone and partook of an acute glomerulitis. These tissue changes again prove the protective influence of the liver against these toxins.

Through *chemical examinations of the products of growth* of B. coli and B. typhosus, especially on sugar media, Duchaceck[2] shows in the presence of air there is more

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(1) Riv. Crit. di Clin. Med., September and October, 1904.
(2) Zentr. f. Bakt., XXXVII, Heft 3.

reduction of glucose to acids, etc., than an atmosphere of carbon-dioxid. Both species attack tartaric acid with avidity, and in about the same degree, but the typhoid bacillus may be somewhat more rapid in its action. Both organisms reduce nitrates to nitrites, which in some way disappear from the media. Upon limiting the amount of air the reducing activity becomes less. When abundance of air is supplied, B. coli produces acetic acid from glucose. B. typhosus produces, under the same conditions, lactic and very little acetic acid. The results of the experiments indicated a difference in degree rather than in kind, except as regards the formation of CO_2, which is peculiar to B. coli.

Paratyphoid. Le Count and Kirby[1] report a case of paratyphoid infection in an infant of 4½ months. The child died, and the examination was made post-mortem. *S. pyogenes albus* was isolated from the bile, meningeal fluid and mesenteric lymph glands and B. coli from a cervical and mesenteric gland. From the liver and a cervical gland a bacillus resembling the typhoid bacillus was obtained. Morphology and growths like typhoid, except that litmus milk becomes acid after 48 hours, and remains so. Gas is formed in glucose-agar and bouillon. No fermentation of lactose, mannite, levulose, saccharose or maltose. Serum obtained by centrifuging the heart's blood agglutinates paratyphoid bacilli, but not typhoid. The serum of a rabbit immunized with the culture isolated likewise agglutinated paratyphoid bacilli and not the typhoid.

Tubercle Bacilli Morphology. Chiese,[2] from an extended study of the morphology of tubercle bacilli in sputa, states there is great variation in cases, and often in the same case. The presence of much mixed infection apparently leads to a more marked morphologic deviation. The bacilli in severe cases were found to be relatively thicker, shorter, and more readily stained. Specimens of sputa were kept in the incubator, and examined from time to time. At first the bacilli increase in numbers, later on show signs of degeneration, and then fail to stain in a characteristic way. By animal experiments it was shown

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(1) Trans. Chicago Path. Soc., Nov. 14, 1904.
(2) Gaz. degli Osped., Aug. 14, 1904.

that the bacilli left in sputum gradually become avirulent, which may even become total in 20 days' time.

The length of time that *tubercle bacilli in dust are capable of causing infection* has been studied by Kirstein,[1] who finds the character of the dust in which the bacilli are has much to do with the result. Comparative tests with *B. prodigiosus* and *staphylococcus albus* show they live longer in dust than in the dried moist particles that have disseminated them. The same was true of tubercle bacilli. In the writer's experiments the material containing tubercle bacilli was not dried *en masse,* but was in the forms of fine dust or floating particles. His general results may be seen from the following table:

VIABILITY OF TUBERCLE BACILLI IN DUST.

Kind of dust.	Period of viability.
Fine particles in artificial dust	Between 8 and 14 days
Tuberculous sputum dust	Between 4 and 7 days
Dried on cloth threads	Between 5 and 10 days
Dried in street dust	Between 3 and 8 days

It would seem that the bacilli are preserved longest in fine dust when infected with the finest moist particles containing them. When the fine particles of moisture ejected during coughing, etc., fall upon smooth surfaces the bacilli die sooner than those falling upon fine dust and becoming mingled with it. The writer thinks that through the drying and disintegration of masses of sputum and the changes during such drying the bacilli are damaged, but where the droplets are deposited on very fine, dry particles desiccation takes place with less injury to the bacilli.

As regards *experimental tuberculosis,* Heymans[1] reports that he has inoculated over 1,000 rabbits with tubercle bacilli from various sources. His observations are of special interest in showing the localization of the infection. Intravenous inoculations were made, and in the animals killed at the end of two weeks or a month practically the only lesions found were in the lungs; in most instances an advanced pulmonary tuberculosis. Animals living longer often showed extension from the lungs and some a general

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(1) Zeits. f. Hygiene, 1905, Heft 2.

(2) Arch. Internat. de Pharmacodynamie et de Thérapie, 1904, fasc. V et VI.

miliary tuberculosis. Retrograde changes were observed in some animals. Healing is apparent in areas of considerable size in one part of the lung, while it continues to extend in another part. Some of the rabbits lived two years and then died of tuberculosis.

Salvia[1] injected cultures of B. tuberculosis into rabbits and then noted the *localization of infection* as regards slight injuries made to different areas. The liver, lungs, ribs, long and flat bones were slightly damaged. In the liver rapidly growing nodules were produced. Hemorrhage did not seem to play an important part in the localization, but it was rather a disturbance of the lymphatic circulation. Localization in the ribs and flat bones usually also caused the neighboring soft tissues to be more extensively infected. Slight injuries to the long bones, their articular cartilages and the synovial membranes did not cause an increased localization at these points. The addition of ammonia here is said to have increased the chance of infection.

Effect of Caffein on Typhoid and Coli. Kloumann[2] tested the direct action of caffein on B. typhi and B. coli. The restraining action was first determined. Ten tubes of agar were taken and to each was added a 1.0 per cent solution of caffein in increasing amounts. The tubes were now inoculated from a typhoid agar culture and the resulting growth observed. The same was done with B. coli.

C.c.f. 1.0% caffein solution.	0	1	2	3	4	5	6	7	8	9	10
Typhoid	xxx	xxx	xxx	xxx	xx	xx	xx	x	—	—	—
Colon	xxx	xxx	xx	xx	x	x	—	—	—	—	—

xxx Active growth. xx Moderate growth. x Slight growth.
— No growth.

The colony count in such an experiment is as follows:

Per cent of 1.0% caffein solution.	Growth in bouillon.	Plates made from bouillon At once.	6 hours.	24 hours.
0	xxx	1,000	1,200	140,000
10	xxx	1,000	1,000	52,000
20	xxx	800	900	6,600
30	xx	900	800	600
40	xx	900	800	1,000
50	x	700	600	800
60	x	800	400	500
70		600	400	140
80		500	500	30
90		500	500	8
100		100	70	5

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(1) Gaz. Med. Lomb., Feb. 6, 1905.
(2) Centralb. f. Bak. I Abt. Orig., Bd. XXXVI, No. 2.

An experiment with colon bacilli is presented not very different from this. These results show, contrary to the statements advanced that the use of caffein causes an increase in typhoid bacilli and a restraint of B. coli, that no such increase takes place without it also occurring with colon. Caffein is slightly more restraining for colon than for typhoid. However, as seen from the table, it is possible to kill colon bacilli before typhoid are completely destroyed. The use of this agent in culture media is therefore not one that assists in the separation of the species by facilitating growth but one that is elective as a restraining agent. When added in proper amount and the cultures made at the right time it can be used to good advantage for this purpose.

The report of Beitzke[1] gives as a result of the *examination of 138 cadavers of children for tuberculosis,* a positive finding in 40 cases. The cases were taken in series as they came to post-mortem in the Berlin Pathologic Institute, with the exception of a few not suitable for the investigation.

Tuberculin; Spray Inhalation. Kapralik and Schroetter[2] report inhalation experiments on 28 cases. It is stated that exactly the same results are obtained by inhalation as by subcutaneous injections. A much larger quantity, however, was required. This was about 30 times the subcutaneous dosage. It was found that smaller doses, causing a reaction, indicated pulmonary infection. In some there was failure to respond to inhalation, but subcutaneous injection was positive. They also report that a certain degree of therapeutic action was seen, and suggest that other biologic products, as diphtheria antitoxin, might be administered in this manner.

Tuberculosis: Destruction and Phagocytosis. Markl[3] injected guinea pigs with virulent cultures of B. tuberculosis intraperitoneally and removed the fluid or exudate found in the cavity by aspiration with capillary pipettes. Cover-glass preparations were made and stained. The results showed that in 3 hours there was evidence of an

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(1) Berl. klin. Woch., No. 2, Jan. 9, 1905.
(2) Wiener klin. Woch., XLII, No. 22.
(3) Zentralb. f. Bakt., XXXVIII, Heft 1.

active chemotaxis, as the bacilli were mostly near the leucocytes. There was also some active phagocytosis apparent on the part of the polynuclear leucocytes. Some of these already contained a considerable number of bacilli. At the 6-hour period there was evidence of increased phagocytosis, and some of the bacilli within the cells did not stain brightly, and were a little swollen.

After 24 hours there was no particular change in the leucocytes, but some of the extracellular tubercle bacilli showed evidence of degeneration and were stained very faintly. In 48 hours the leucocytosis had decreased, and only an occasional leucocyte containing bacilli could be found. These cells showed marked evidence of degeneration. Some extracellular bacilli stained well, but there were many that showed only a faint rose color.

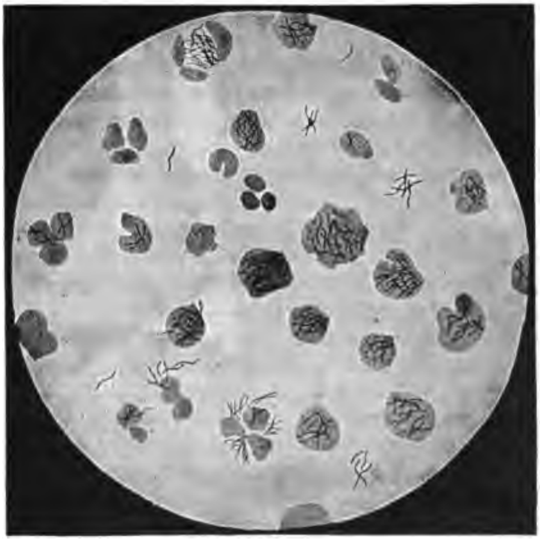

Fig. 16. Tubercle bacilli undergoing inclusion by phagocytes.

At the 72-hour period mononuclear leucocytes became numerous. The presence of normal shaped and staining extracellular tubercle bacilli could now no longer be demonstrated. Later observation showed that the leucocytosis decreased, and that scarcely any extracellular tubercle bacilli could be found, but that here and there intracellular small numbers were present. At first in the infection there is evidence of an active defensive process.

The question of the *relation between human and bovine tuberculosis* continues to excite interest and several articles present experimental evidence bearing on this subject. Dammaren[1] describes the results of successful inoculation of a human strain of tubercle bacilli in calves and hogs. This culture was obtained from a case of peritoneal tuberculosis in a woman. Guinea-pigs were inoculated from the patient, from these pure cultures were obtained. A pig was inoculated subcutaneously with the cultures, and from the lesions in this pig, a calf and another pig. The animals died of generalized tuberculosis in 28 and 42 days respectively. All possible precautions were used to keep

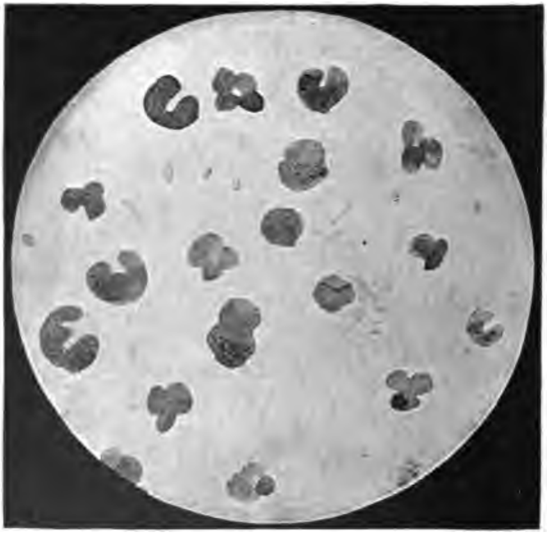

Fig. 17. Bacteriolysis of tubercle bacilli.

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[1] Deut. tierarztl. Woch., 1904, No. 53.

the animals used in the experiments free from bovine or other tuberculosis. In fact, the results observed in the larger animals were so similar one would at once recognize that the same strain of organism was active in all.

Preisz[1] inoculated 17 beeves with a mixed culture derived from guinea-pigs which had been infected from human sputum, lymph glands and lung tissue. In all there were bacilli from 10 different human sources. They were inoculated subcutaneously and intravenously, while at the same time other beeves were fed tubercular sputum for several months. The writer found that none developed generalized tuberculosis. Local lesions were the rule but in some instances the neighboring lymph glands became involved. The 2 control calves were fed with the tissues from tuberculous cattle and later inoculated intravenously. Only one of these became infected.

From these results it would seem that something more than the application of tubercle bacilli is necessary to produce infection. Preisz agrees with other observers that age, nature of the animal's food, and general health condition, influence this to a large degree. The inference is drawn that in dissemination of human tuberculosis the same general influences may be operative.

Raw[2] summarizes his observations on human and bovine tuberculosis in about 3,000 cases and 600 necropsies. He believes pulmonary infection in older persons is due to inhalation of dried sputum or moist particles. Only a few are secondary to cervical tuberculous adenitis. In children there may be extension from mesenteric glands through the diaphragm. Such infections may be milk infections. He is inclined to agree with Koch's view that human and bovine tuberculosis are sharply differentiated. He believes man can be infected from cattle, though this is relatively rare, and further that bovine tubercle bacilli do not cause the typical characters of human tuberculosis.

There are reported 293 cases of tabes mesenterica diagnosed by the author. None of these were found to be breast-fed exclusively, but received cow's milk in part or

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(1) Zeits. f. Tuberculose, 1904, Heft 3.
(2) Tuberculosis, 1904, No. 11.

entirely. Cases of healed mesenteric gland tuberculosis were found, these, like cervical glands, are considered due to milk infection and may all recover spontaneously.

The geographic distribution of tuberculosis is also discussed. The general rule is that infant tuberculosis is less or practically unknown in those countries where cattle tuberculosis is absent or infant feeding with sweet milk is not practiced. The conclusion is that the infection with bovine bacilli in childhood results in a degree of immunity, and that later such children are free from pulmonary consumption. In fact, such mild attacks are equivalent to vaccination and in cases where the damage is slight assist in protecting against the more dangerous human person-to-person infection.

The inoculation experiments of de Yong[1] were stimulated by the Koch theories regarding the *difference between human and bovine tubercle bacilli.* That there is a difference in virulence between the two is recognized. The human cultures are much less virulent.

The following is one of the series of experiments performed:

Control Pure Culture from Kidney.—A 2½-month calf inoculated intravenously May 8, 1900, did not die. Goat inoculated intravenously April 3, 1900, dead August 26, 1903. Guinea-pig inoculated with, died November 21, 1903.

Culture from guinea-pig inoculated subcutaneously into goat January 16, 1904, dead February 19, 1904.

Mediastinal gland inoculated subcutaneously into calf February 19, 1904, dead March 9, 1904 (mixed infection).

Inoculation of guinea-pig March 9, 1904, dead April 24, 1904. Cultures made.

Subcutaneous inoculation of calf with guinea-pig cultures July 9, 1904, dead August 3, 1904. (This calf showed a generalized tuberculosis.)

From April 3, 1900, to August 3, 1904, with passage through 6 animals, and twice in pure culture, this strain isolated from man had developed a degree of virulence entirely equivalent to that of a bovine type.

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(1) Zentralb. f. Bakt., XXXVIII, Heft 2-3.

Karlinski[1] experimented upon Bosnian cattle because of the well known relative immunity of this breed towards tuberculosis. He used cultures from guinea-pigs which had been inoculated with human sputum. Some of the cultures had been through the guinea-pigs more than once. The results showed positive infections in 13 of the 14 animals inoculated. The results were such that no difference between the infection in ordinary cattle could be seen. The use of guinea-pig passage and intravenous injection will overcome the natural immunity in these animals.

Figori[2] decided from his experiments that *immune bodies could be transferred to the young through milk.* This confirms several earlier observers, and especially Maragliano. The young of cows and goats actively immunized against tuberculosis show a certain degree of immunity from the parent at the time of birth. Later this is increased through the milk absorbed. In like manner adult animals show that milk containing immune bodies will increase the degree of immunity of the animal's serum.

Smidt[3] reports his results of tuberculin injection in a number of cases likely to come to necropsy. Among a considerable number injected. 10 came to necropsy. Of these 5 showed confirmation of the test. Two were found entirely free from tuberculosis. One that had given a negative result showed tuberculosis present. One was a case of leprosy with probably latent tuberculosis; here extensive recent tuberculosis was present, indicating that bacilli had been liberated. The last was one of extensive tuberculosis in which the disease was disseminated owing to the reaction.

The use of *muscle plasma* from immunized animals is proposed by Pallieri[4] in the treatment of tuberculosis. His experiments show these extracts have a bactericidal, as well as an antitoxic action towards the tubercle bacillus.

The Passage of Tetanus Poison Along Nerve. From his experiments Tiberti[5] concludes that when tetanus toxin

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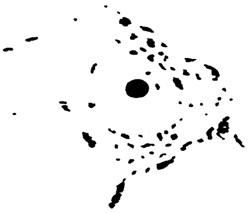
(1) Zeits. f. Tiermed., 1904, Heft 1 and 2.
(2) Riforma Medica, April, 1905.
(3) Zentralb. f. Bakt., XXXVIII, Heft 6.
(4) Muench. med. Woch., 1904, No. 18.
(5) Gazetta degli Ospedali, XXV, No. 136.



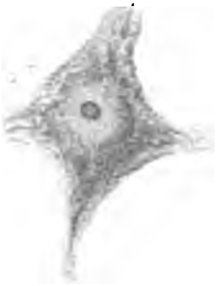


Fig. 4.

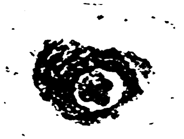


Fig. 5.

Fig. 6.

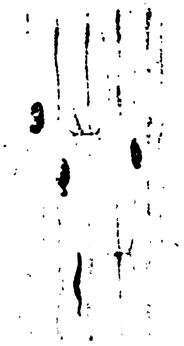
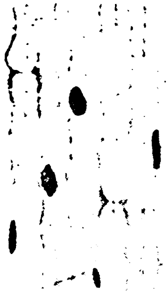


Fig. 7.



is injected subcutaeonusly into a susceptible animal, the major portion is taken up by the lymphatics into the blood; a small portion is absorbed along the nerves to the central nervous tissues. When the injection is made into a limb it is possible to find the toxin continuously present in the nerves of that limb. Absorption does not take place along the lymphatics of the nerves, but along the protoplasm of the axis cylinders, moreover this must be normal.

The toxin moves only in the direction of arrangement of the nerve cells. Apparently as lower cells become saturated those above tend to attract the poison. When the toxin is injected into a muscle it spreads out into the surrounding serous fluids, and later is taken up by the nerve endings and absorbed centrally. Symptoms of tetanus poisoning can be induced by the injection of minute amounts of toxin directly into nerves, while the same amount injected subcutaneously would not cause them. When tetanus antitoxin is injected into a nerve trunk, the subsequent injection of toxin into the muscles supplied by this trunk does not cause tetanic symptoms; the progress of the toxin being stopped. As the toxin reaches the centers through the nerves, it is possible by cutting the cord to prevent damage to higher centers, or regions of the cord by extension. The injection of toxin subsequent to cutting a nerve trunk will not induce contractions in the set of muscles involved. When the toxin is directly injected into the cord the incubation period is short. When injected into the circulation all muscles become involved simultaneously, and local manifestations are absent. Such intravenous injections lead to a rapid transfer of the toxin from the blood to the lymph.

Fig. 18. Action of Tetanus Toxines—Tiberti.

Fig. 1. Normal cell from anterior horn, rabbit.

Fig. 2. Granular chromatin degeneration of such cells in tetanus infection.

Fig. 3. A similar cell from infected guinea pig.

Fig. 4. Cell from rabbit showing vacuoltation of cytoplasm.

Fig. 5. Cell from the cord of infected guinea pig showing neuroglia granules.

Fig. 6. Sciatic nerve of infected rabbit stained by Bethe's method, fairly good staining of axis cylinders.

Fig. 7. Sciatic nerve showing poor staining due to tetanus.

A case of tetanus treated by Mornac[1] by *epidural injections* of tetanus antitoxin was not saved. The case was not treated until the fourth day of the convulsions. The writer considers the method advisable, and, because it is simple, recommends its use. Antitoxin must be given early enough to expect a cure. A few cases treated in this way are reported as having recovered.

Trachoma Bacteriology. Knapp[2] made bacteriologic examination of 120 cases of trachoma, and found in 8 a bacillus resembling B. influenzæ and the Mueller trachoma bacillus. The organism was small, had rounded ends, stained with difficulty, and grew only on hemoglobin-containing serum. The colonies were "dew-drop" in character. No pathogenesis could be demonstrated on animals. The writer considers this organism accidental, and strengthens his position by recognizing an influenzal conjunctivitis without there necessarily being other mucous membranes involved.

Syphilis Spirochæte. Schaudinn-Hoffmann[3] report finding a peculiar spirochæte in the fluid of syphilitic lymph glands. These can be demonstrated on the surface of syphilitic papules and primary sores, and also in the tissues when stained with azure blue and eosin. Two organisms are recognized, each of which has been given a name. A darker staining, larger organism, *Spirochæte refringens;* and a smaller, lighter staining organism, *S. pallida.* The latter alone was found in the deeper tissues. Twenty-six patients have been examined so far, and all gave positive results. The organism is extremely delicate, almost transparent and actively motile. It is thread like and spiral; it varies from 4-14 u in length and .25 u in thickness. From 6 to 14 curves are present. In S. pallida the curves are sharper and more numerous than in refringens.

It is not claimed a causal relation to syphilis has been demonstrated. The workers at the Institute Pasteur who examined some of the original specimens found the organ-

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(1) Presse Médicale, 1905, No. 12.
(2) Archives of Ophthalmology, September, 1904.
(3) Deut. med. Woch., May 4, 1905.

ism in 4 out of 6 apes inoculated with syphilis. (Report to Academy of Medicine, Paris, May 16, 1905.)

Metchnikoff and Roux[1] assert that *syphilis is a chronic spirillosis* due to the Schaudinn *Spirochæte pallida.* They state it was present in 8 cases in man and animals, but could not demonstrate that it was alive. The examination of non-syphilitics was negative. A stain to demonstrate it rapidly consists of azure blue in methyl alcohol, with a weak aqueous solution of eosin. Blood films are stained with this mixture.

Risso and Cipollina[2] *treated cases of syphilis with the serum of dogs* which they had injected with blood taken from persons in the secondary stage of syphilis, subcutaneously and intraperitoneally. The animals were injected every six days for a number of times, and bled a week after the last injection. The only results noted were due to hemolytic action when the amount of blood injected was too large. In treatment from 2 to 5 c.c. of dog serum were injected into a muscle every day at first, and later at longer intervals. Sixteen cases are reported, 14 secondary and 2 tertiary. Nine of the former are reported as cured, and the two latter also. Other cases are under treatment. The results warrant the assumption that the immunity of refractory animals can be raised.

Vaccine Cytology. Prowazek[3] records the following observations on vaccine at the protozoan laboratory of the German Imperial Health Department: Direct microscopic examination of lymph specimens showed round, oval or sharply outlined bodies in large numbers in the cell fragments present. These he calls "lymph bodies." The method used consisted in fixing with 2/3 concentrated bichlorid solution and 1/3 90 per cent alcohol. Staining by diluted Grenacher's hematoxylin. Inoculation of the cornea of rabbits was accomplished by placing minute drops of diluted vaccine on sharp splinters of cover glass. These were examined with high power and if satisfactory the inoculation was made by piercing into the cornea. Dilution experiments were also made. At 1:1000 potency

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(1) Bull. Academie de Méd., LXIV, No. 26.
(2) Riforma Medica, November, 1904.
(3) Deut. med. Woch., 1905, No. 19.

was still manifest. Line inoculations across the cornea showed cloudiness at first, further along this appeared only in spots. The lymph filtered through folded filters was more or less active when inoculated into the cornea.

According to Siegel there are motile bodies in vaccine lymph. In order to settle this point some diluted lymph was carried by a capillary tube into the bottom of a pointed centrifuge tube filled with salt solution. The overlying fluid was now inoculated from various levels by corneal implantation. Small tubes closed by filter paper were also placed at the bottom of centrifuge tubes, and the supernatant liquid again examined. In none of these experiments were motile bodies present.

After inoculation of the cornea of rabbits Guarnieri's bodies were present in increasing numbers as early as the third hour, but besides there are bodies 1-1.5 *m.* in length, oval, with a light zone within them containing a pair of chromatic granules usually of unequal size. These are best demonstrated by staining sections with saffranin, dahlia or gentian violet, then applying 10 per cent watery solution of tannin followed by 1 per cent solution of antimony tartrate.

The Guarnieri bodies are not the parasite as shown by Foa, in that a 10 per cent salt solution applied to lymph damages them severely, and yet such lymph will be potent upon inoculation. Reagents which do not damage encysted protozoa will not render lymph inert. These bodies are specific for vaccine material and have some resemblance to the Negri bodies found in hydrophobia.

Inoculation does not give a cycle of development, but the results of inoculation are the same at all times from 8 to 336 hours. The distribution of the organism in the epithelium is not confined to the cell protoplasm but appears intracellular also. An experiment described would seem to prove this. If a 16-hour-infected cornea is laid in a capsule for 10 hours, one may shake from it numbers of cells by agitation in salt solution. If the resulting liquid is filtered, positive results can be had with the filtrate. When the cells now remaining on the paper are partially digested with trypsin they discharge some of the bodies, and the filtrate again prepared becomes potent. Inoculation experiments show the other eye can be infected for a period of 2 months, but the same eye after recovery apparently has immunity. It has been possible to propagate virus in this way, as many as 46 generations having been successfully cultivated.

L. Voight[1] has succeded in raising a *fresh stock of variola vaccine.* Although the Lyons Commission in 1863 decided that smallpox could not be transferred to the cow, it has nevertheless been accomplished several times in Germany, Switzerland and England. In 1881 Voight succeeded in this in the Hamburg State Institution, and the lymph was used with success. The new stock as reported was obtained by inoculating rabbits with an emulsion of smallpox crusts in glycerin and then shaving off the nodules, and inoculating calves with this material. After the third removal from the calf the lymph was used for primary vaccinations with good success. At first the vesicles appear much more slowly.

Carini[2] proceeds as follows in the examination of vaccine for B. tetani: Spores of the bacillus are most important because the vegetative forms are killed by the glycerin or other preservative used. Bulbs with long capillary outlets are prepared and partly filled with sterile bouillon. Into these several drops of lymph are drawn and mixed with the bouillon. By this means the tubes can be exhausted as much as possible by the vacuum pump and sealed; some are now heated to 176° F. for a few minutes, and some are not. All the tubes are placed in the incubator for a week or two, in order to allow the spores to sprout and the bacilli to increase. Guinea-pigs are injected if there is any evidence of suspicious organisms present. In 400 tests of lymph from 50 different sources, B. tetani was present 5 times. The results indicated that tetanus must be considered in the flora of vaccine. The number found should not be considered alarming. Some specimens examined and found to contain tetanus were used successfully in a large number of vaccinations. The writer

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(1) Monatsh. f. prak. Dermatologie, 1905.

(2) Zentr. f. Bakt., 1903, Heft 1.

suggests that great cleanliness alone can prevent the presence of tetanus, and that in the practical conduct of vaccinations only superficial scarifications be made and not injections into the tissue.

Pathogenesis of Cancer. Maniscalco[1] reports having produced a condition like cancer in dogs by chemical and mechanical irritation of the stomach. This causes inflammatory changes, and as long as the epithelial cells can be readily exfoliated no cancerous changes appear, but if there is any impediment to removal, the epithelial cells spread to the deeper tissues. The writer did not continue the experiment sufficiently long to eliminate repair in his animals. The investigation seems to show that the glands are starting points for carcinomas. Even in blastomycosis it would appear that irritation precedes the epithelial changes.

METHODS.

Solid Medium for Cholera. Hirschbruch and Schwer[2] prepare a culture medium for plating from the primary peptone-salt solution, used for the isolation of cholera, after the following method: 125 c.c. ordinary nutrient agar, melted and added to 1.5 gram lactose; the mixture is boiled for 15 minutes. Now there is to be added: Azolithmin, .04 gram; crystal violet (1 per cent), 1 c.c.

The mixture is boiled again and cooled to 113° F. and poured into Petri dishes. These are inoculated by spreading drops lightly over the surface. The medium must be nearly neutral so as to give the colon bacilli opportunity to make red colonies and at the same time to allow the cholera spirilla to grow.

The *addition of calcium salts to media* for cultivating the pneumococcus or meningococcus is proposed by Bolduan.[3] The well known interference of acid and sugars from which acid is formed, on the active growth of pneumococcus led him to look for some method to neutralize the acid as formed. At first he added powdered calcium carbonate, later on pieces of marble. Under ordinary con-

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(1) Rif. Med., April 1, 1905.
(2) Zentral. f. Bakt., XXXVI, No. 1.
(3) N. Y. and Phila. Med. Jour., May 13, 1905.

ditions where pneumococcus cultures are transferred they soon die, or very large amounts must be transferred to keep them alive.

The writer's observations show the addition of pieces of marble make it possible to transfer cultures without interrupting growth. To see if it was entirely due to neutralization of the acid, other salts were used. From the results it seems that minute quantities of calcium facilitate growth, and that the neutralization of acid assists to a considerable extent. In plate cultures calcium chlorid (0.1 to 0.5 per cent) is best, as it does not make the plates opaque.

The *staining of protozoa,* as proposed by Marino, is discussed by Giemsa,[1] who himself recommends the following:

Azur II—Eosin	3.0 grams
Azur II	0.8 grams
Glycerin	250.0 grams
Water	250.0 grams

Specimens are fixed with wood alcohol, then stained with a dilute solution of the above 1 drop to each c.c. of water for 15 to 30 minutes.

Gabrielides[2] reports a rapid stain for tubercle bacilli. His modified Ziehl formula is as follows:

Fuchsin	1 gram
Alcohol	10 c.c.
Phenol	5 grams
Water	40 grams

The stain is heated on the slide and decolorized with 25 per cent nitric acid in alcohol. It is stronger, and the decolorization is instantaneous. Counter-staining is done with methyl blue.

Wile's method[3] *for tubercle bacilli* consists in staining films of sputum or smears prepared as usual, with warm carbol fuchsin and after draining quickly, the slides are plunged into Labarraque's solution, until the slide has a uniform brownish hue. It is then washed in distilled water, and dried with paper. The tubercle bacilli stain red on a brown field. Others are brownish, but acid-fast

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(1) Annales de l'Institut Pasteur, 1905, No. 5.
(2) Grèce Médicale, IV, No. 23.
(3) N. Y. and Phila. Med. J., Jan. 28, 1905.

bacilli retain the original color the same as the tubercle bacilli.

Acid-Fast Bacilli. Piatkowski[1] reports that *acid-fast bacilli* are so resistant to formalin it can be used as a means of separation from other bacteria. He also states their staining properties are not injured. [It is well known that formalin is a mordant in some instances in stains. One of the earliest workers to recommend it for this purpose was A. P. Ohlmacher.—Ed.] His method is to mix the material in 10 c.c. of water, and add 1 or 2 drops of formalin. The tube is well shaken and at intervals of 15 minutes drops are transferred to glycerin-agar or blood serum, and cultivated. The first inoculated tubes may not grow, but if transferred again, a pure culture will be obtained. The writer also uses this method for the rapid separation of any weaker from a more resistant organism.

An elective stain for spores is described by Scagliosi[2] as follows: Slides spread as usual are fixed in Van Gehuchten's fluid for 30 minutes, then stained with Ziehl's fuchsin, rinsed in water and counterstained with methylene blue. The latter is especially good.

The *staining of flagella of motile bacteria* is accomplished by Duckwall[3] by use of a mordant and carbol-fuchsin stain. The mordant is prepared by dissolving 2 grams tannic acid in 15 c.c. distilled water, and adding 5 c.c. cold saturated solution of ferrous sulphate and 1 c.c. concentrated alcoholic solution of fuchsin. Solution of sodium hydrate is added according to the results obtained. This mordant must be used in a few hours as it does not keep. The preparations to be stained must be from a young culture, spread thinly over a large surface and fixed with as little heat as possible. The mordant is next applied and heated very gently. Rinse in water, and quickly in absolute alcohol. The carbol fuchsin is now applied and heated to steaming, wash, clear in xylol and mount.

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(1) Deut. med. Woch., XXV, No. 24.
(2) Riforma Medica, XX, No. 49.
(3) N. Y. and Phil. Med. Jour., June 24, 1905.

The following procedure for *capsule staining* is recommended by Buerger[1] as giving excellent results:

1. Fix specimens, when almost dry, in Mueller's fluid saturated with bichlorid.
2. Heat gently.
3. Wash in water.
4. Wash in alcohol.
5. Tincture of iodin, 1 to 2 minutes.
6. Wash in alcohol.
7. Stain with anilin-water-gentian violet.
8. Mount and examine in 2 per cent salt solution.

When cultures are to be examined the films should be spread with a drop of blood serum or other albuminous liquid.

As regards the *stain for spongioplasm,* Unna[2] states the important element in polychrome methyl blue is a combination of the blue with an alkaline carbonate forming methylene azure-carbonate. The addition of methyl violet adds more carbonates and increases the staining properties for spongioplasm. The formula presented contains:

Potass. carbonate	.25 parts
Azure carbonate	.25 parts
Methyl violet	1.00 part
Water, to make...........	50.00 parts
Glycerin, to make.........	50.00 parts

Ruata[3] reports on *Endos' differentiating test* for typhoid bacilli:. This consists in growing the bacilli on a medium containing fuchsin decolorized by sodium sulphate. This medium is transparent and shows the typhoid colonies colorless, while the colon bacillus causes the red of the fuchsin to return. Comparative tests of the method did not show that it had special advantages over others.

In *testing for rabies* Ohlmacher[4] recommends that in place of the usual chipping away of the calvarium it be sawed through. The saw is entered midway between the auditory meatus and the orbit, sawing clear through at right angles to the cerebrospinal axis. The tentorium can

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(1) Medical News, Oct. 10, 1904.
(2) Monatsh. f. prak. Dermatol., XLII, No. 3.
(3) Riforma Medica, 1904, No. 16.
(4) Jour. Amer. Med. Assoc., Sept. 10, 1904.

be cut away, the cerebellum raised and portions of the medulla easily cut out. For microscopic test (Van Gehuchten) the writer prefers the Gasserian ganglion, as this is large, and also can be readily removed. He fixes in absolute alcohol or Carnoy's acetic acid-chloroform-alcohol-mixture. Formalinized portions of the ganglia can be frozen, cut immediately and stained.

Test for Albumin. Ravold[1] prepares a *reagent for albumin* as follows:

Sat. sol. sulphate of magnesia	50 c.c.
Mercuric chlorid	2 grams
Succinic acid	4 grams
Sodium chlorid	4 grams
Water	50 c.c.

The urine is acidified by adding 1 c.c. acetic acid to 5 c.c. urine and filtered. The urine is now allowed to overlay the reagent in a test-tube. Should there be a ring at the point of contact, heat will not dissolve it when it is albumin. The test is reported as being very delicate and free from fallacies.

Mann[2] considers the *orcein test for sugar* in the urine (Neumann) as very simple and reliable.

Ogden[3] finds boric acid to the amount of 5 grains per 4 oz. is to be recommended as a *preservative for urine.* This determination is based on experiments with 140 samples of urine of widely divergent character.

ALLIED ORGANISMS.

Ankylostomiasis. Lambinet[4] experimented on dogs with A. caninum. The larvæ of this species were inoculated by feeding, application to the surface of the skin, and subcutaneously. The author found infection took place with each of these portals of entrance. All larvæ injected subcutaneously arrived rapidly in the intestine; of those placed on the skin only part localized there. He finds the seat of election of these parasites is not the duodenum,

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(1) Jour. Missouri State Med. Assn., April, 1905.
(2) Berl. klin. Woch., Feb. 27, 1905.
(3) Boston Med. and Surg. Jour., June 22, 1905.
(4) Bull. Acad. Med. de Belgique, Jan. 28, 1905.

a view of producing artificial infection with ankylostoma but the middle and upper small intestine. It requires some time for the larvæ to become adult after reaching the intestine (in most cases about three weeks). It was further found this time was about the same whether the larvæ were applied subcutaneously or by the mouth.

Experimental Trypanosomiasis. Halberstadler[1] transferred blood from mice infected with trypanosomes to other mice and rabbits. Blood was taken from the tip of the tail and injected intraperitoneally. It was diluted with normal salt solution, and less than 1 c.c. injected. After 24-48 hours the organisms appeared in the blood. The animals died in 4-6 days without apparent evidence of pathologic changes. He remarks that the finding of motionless trypanosomes does not necessarily mean they are avirulent. Upon transferring such specimens to the peritoneal cavities of mice all evidence of virulence is manifest. It would seem the organisms revive under the new conditions of transplantation. The resistance of these organisms is considerable, as shown in experiments by Laveran and Mesnil, who found that —375° F. for 25 minutes under liquid air, and 105° F. applied for 1 hour did not kill all the organisms. Most of them became misshapen, and the degenerations caused may account for the longer incubation period after injection of such specimens to 14 days or even 3-4 weeks.

Blood Leucocytozoan. Bentley[2] makes a preliminary report of finding a parasite in the leucocytes of dogs. The blood of a number of English dogs raised in Assam, India, was examined. The animals showed slight anemia and slight fever. Blood films stained by Romanowski's stain showed numbers of polynuclear and transitional leucocytes to contain one or more oval, nucleated bodies. They gave the appearance of being contained in a capsule in which there was a nucleated mass. The contour and position of the nucleus was unusual in most instances. In fresh specimens the parasite appeared as a rod-like body lying upon, and sometimes to one side of the nucleus.

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(1) Zentralb. f. Bakt., XXXVII, Heft 5.
(2) British Med. Jour., May 6, 1905.

The writer concludes it is a hemogregarine. If this is true, it is probably the first instance in the blood of a mammal.

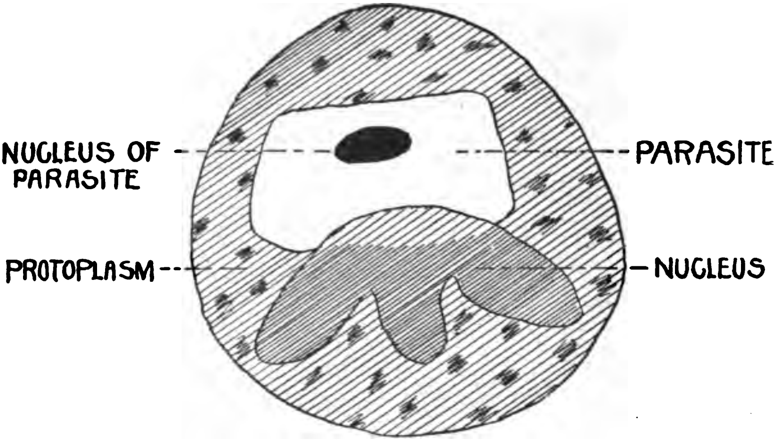

Fig. 19.

A New Blood Fluke of Man. Schistosoma Cattoi. Catto[1] among numbers of coolies found one infected with this fluke. Further investigations of tissues and specimens were conducted at the London School of Tropical Medicine. At the necropsy much superfluous fat was noted, the lower intestines were much thickened and cut with a gritty feeling. Higher up this condition occurred in patches. The liver showed a coarse cirrhosis, giving an irregular, knotty surface and thickened irregular border. Sections of the intestinal wall, liver and mesenteric lymph glands showed numerous oval bodies with a smooth stout capsule. Opinion differed as to whether these were coccidia or the ova of some unknown parasite. During the investigation of the tissues, ova and embryos were found in

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(1) Brit. Med. Jour., Jan. 7, 1905.

smears from the intestinal contents and one in the vessel of a mesenteric gland.

Subsequently, in sections of the mesocolon adult trematodes male and female were found in the blood vessels, and with ova (like those in the intestine) in the uteri of females. Although not as yet definitely settled it appears to the author that the worms occur in both veins and arteries. The male as found in alcohol specimens measures 9 m.m. long by .5 m.m. broad. There is a gynecophoric canal as in Schistosoma hematobium. The anterior extremity is blunt with a terminal sucker in which the mouth lies. The posterior sucker is larger and more muscular. The female is almost cylindrical and longer, more slender and darker. The eggs are oval 70 u by 40 u. They have a stout, smooth shell, without spine or operculum.

The ulcerative lesions in the bowel show absence of fungating masses so characteristic of *S. hematobium.* The parent worms are found at the bifurcation of the mesenteric vessels where they form plugs more or less complete. Where ova accumulate they provoke a small cell infiltration which later gives place to a marked fibrous tissue proliferation. The ova are plentiful in the liver, mesenteric glands, stomach and intestinal walls. Filiform embryos and ova are found in the feces and in scrapings from the intestinal mucosa made post-mortem.

Plasmeba of Dengue. Eberele[1] has named the organism that he reports in the blood of dengue cases "Plasmeba." He states it is in the plasma and later attacks the corpuscles, leading to the formation of irregularly shaped violet-tinted growths, with a few dark granules; spores may also be seen. These are formed in the corpuscles and are discharged by rupture of the remaining film of stroma covering them. The spores now begin a new cycle. The plasmeba is smaller and more active than the malaria plasmodium, there are no crescent shapes or flagellate bodies to be seen. There is no enlargement of the spleen, and the organisms can be demonstrated in all stages during the sickness. Quinin was found to have no effect upon the organism.

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(1) N. Y. and Phila. Med. Jour., Dec. 24, 1904.

Filaria. Mon and Carballo[1] report the finding of a single specimen of *Filaria Bancrofti* in the blood of a man who suffered from nocturnal hemoptysis. Under the administration of iodin all symptoms disappeared and the patient has remained healthy.

Filariasis and Yaws. Boissiere[2] reports on the distribution of this disease in Fiji: Almost every adult can report to have been afflicted at some time. The tertiary manifestation of yaws are ulcers that heal only with difficulty. They may appear on any part of the body and are usually foul smelling. Granulations of the palms and soles are also seen. Yaws and syphilis are closely related, although the former seems to confer immunity against syphilis. The treatment with potassium iodid would indicate that it is syphilis or has a very close relation to that disease.

Piroplasma Hominis. Craig[3] calls attention to certain areas in erythrocytes which are devoid of hemoglobin as having been mistaken by Chowning and Wilson as a protozoan parasite in spotted fever. It would seem such areas occur in the course of many conditions, and that their causes or indications are not known. Further, Stiles, with others, examined the blood in cases of spotted fever without finding protozoa present.

Malaria Antitoxin. Ford[4] prepared an antitoxin to be used in the treatment of tertian malaria. Rabbits were injected with the blood of malaria patients or the animals were bitten by infected mosquitoes. The antitoxin from the rabbits was in the form of fluid serum, defibrinated blood or corpuscles desiccated and again dissolved in salt solution.

Nine cases of malaria were treated with these preparations, 2 were not influenced, 1 showed temporary disappearance of symptoms, 1 developed an abscess, 4 recovered after a time and showed rapid disappearance of the parasites.

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(1) Revista de Medicina y Cirurgia, 1905, No. 23.
(2) Jour. of Tropical Medicine, June 15, 1904.
(3) American Medicine, Dec. 10, 1904.
(4) Medical Record, Dec. 24, 1904.

DICTIONARY
OF
NEW MEDICAL WORDS

BY

WILLIAM HEALY, A. B. (HARV.) M. D.

INTRODUCTORY NOTE.

These 370 words have been gathered from the literature of the year and tell something of the tale of medical progress for that time. They are arranged as those in previous editions, with phrases under the head of the principal noun, thus hepatic siderosis under siderosis.

New Dictionary Supplement

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THE YEAR BOOK PUBLISHERS.

Aggressin. A hypothetical substance which by action on the polynuclear leucocytes prevents phagocytosis and so renders invading bacteria more aggressive.

Ailurophobia. [Gr. ailouros, a cat.] The fear of cats.

Akaralgia. A combination of sodium salicylate, sodium and magnesium sulphate, nux vomica, etc. Used for the treatment of migraine, etc.

Akarkine. An albuminate of arsenic. Used in treatment of cancer.

Albaigin. A combination of silver nitrate with gelatose, containing 15 per cent silver. Only slightly irritating to mucous membranes.

Alka-men-thym. An alkaline, antiseptic solution containing boric, benzoic and salicylic acids with eucalyptol, glycerin, etc. Used as gargle, spray, etc.

Antemesin. A compound c
anesthesin. Used in trea
sea, gastric ulcer, nervou
sia, etc.

Antiabrin. An antitoxin
blood corpuscle poison of
rity bean.

Anticrotin. An antitoxin fo
toxin from the bean of c
lium.

Antileucocidin. An antitoxi
leucocytic poison of the
coccus.

Antiphlogin. A synonym fo
rin.

Antiputrol. Antiseptic c
large percentage of phenol
congeners.

Antiricin. An antitoxin for a
corpuscle poison of the c
bean.

Antirobin. An antitoxin for robin, a locust tree poison.

Antitoxin, Normal a. The standard of antitoxin strength: 0.1 c.c. of it will protect a guinea pig of 250 grams against 100 lethal doses of toxin.

Antiurease. An antiferment for urease, a urea splitting ferment.

Antivom. A preparation of anesthesin used to prevent nausea.

Apergols. Proprietary capsules containing apiol, ergotin, oil savin and aloin.

Apnol. Liquid containing periplocin as the active agent. Remedy for asthma, used by inhalation as spray.

Apophysitis. A name proposed to replace the term appendicitis.

Argentose. Soluble organic silver compound. Astringent and germicid.

Arhovin. Product of combining diphenylamine and thymol-benzoic acid ester. Dose: 5 minims in gelatin capsules for gonorrhea.

Ascaris texana. A variety of intestinal parasitic worm recently observed in Texas. It is differentiated from other varieties by the possession of a toothed anterior labial border and interlabia, etc. Length about 60 mm.

Ateleiosis. [Gr. ateles, incomplete.] Infantilism. The retention to adult age of general infantile characteristics with or without sexual maturity.

Atrophy. Hoffman's a. A form of progressive muscular atrophy attacking the legs below the knees and later the forearms and hands. The Charcot-Marie-Tooth syndrome.

Autoprecipitin. A precipitin which proves active against the serum of the animal in which it was formed.

Azoimid. A protoplasmic poison resembling in its action hydrocyanic acid. Made from hydrazin.

Azotorrhea. The discharge in the stools of abnormal quantities of nitrogenous food, the result of faulty digestion of albumin. This may be a symptom of pancreatic disease.

B

Bacillus maternus. A very large non-motile facultative anaerobe. Seen occasionally in sputum, smegma, etc. So named because possibly it is a mother-shape of tuberculosis bacillus.

Benolgur. A preparation of benzoic acid and gurjun oil used as urinary antiseptic, etc.

Benzo-kinone. A non-caustic soluble derivative of guaiacol. Dispensed in a syrup-elixir containing 2 grains to the teaspoonful.

Betul-ol. A preparation of salicylates in oil as a vehicle for administration through cutaneous surfaces.

Bionergy. The underlying life force or vital energy which is the foundation of all organic life.

Bioplasmine. A hypothetical substance contained in every living cell and which is necessary to the functioning of the cell, but which becomes exhausted, progressively diminishing metabolic activity.

Bioplasminogen. A hypothetical substance from which bioplasmine is formed during embryonic growth and which is itself derived by the union of specific substances, the so-called spermatoplasmon and ovoplasmon, in the elementary male and female cells.

Bioplastin. An egg-yolk preparation containing lecithin and iron.

Bioson. Nutrient containing iron, albumin and casein. Dose: 1 to 2 ounces daily.

Bismon. Colloidal bismuth oxid, containing 20 per cent bismuth. Soluble in water. Dose: 7 grains in 10 per cent solution four times a day.

Blandine. A neutral, odorless mineral oil used as a base for medicaments.

Bocaral. Compound powder of boric acid, alum, carbolic acid, etc., used as antiseptic dressing.

Borneol salicylate. The same as salit, q. v.

Bradyphagia. Eating too slowly.

Bronchol. A combination of terebene, oil of sandalwood, creosote, eucalyptol and strychnine. Put up in capsules for chronic bronchitis.

C

Cacodol. An organic arsenic compound, used as tonic reconstructive in phthisis.

Calcidin. Iodized calcium. An amorphous combination of iodine and calcium given in frequent doses of 1-3 to 1 grain for croupous conditions.

Calomelol. Soluble, colloidal calomel used as dusting powder or in ointment.

Candol. A dry extract of malt. A starch digestant and nutrient.

Capillin. Condensation product of tannin, chloral and resorcin. For treatment of seborrhea, etc.

Carbenzol. An oily product obtained from distilling certain mineral oil deposits. A specific for skin affections dependent on local parasitic action.

Cellotropin. Monobenzoyl-arbutin. Used for treatment of tuberculosis and scrofula. Dose: 5 to 7 grains.

Cellulo. A combination of glycerin, oxychlorine, cellulose, with an earthy base. A highly absorbent plastic dressing.

Chevadol. Terpin iodohydrate. Antiseptic dressing powder.

Chil-Cedine. A combination of Warburg's tincture, Fowler's solution, iron peptonate, cascara, and potassium iodide. For malaria.

Chlorhydromethylarsenate of lithium. An arsenical preparation used in aqueous solution.

Chloro-bromon. Alkaline, antiseptic liquid for treating mucous membranes, etc.

Cholecystopexy. The surgical fixation of the gall bladder to the abdominal wall.

Cholelithurin. A preparation of fresh bile used in treatment of cholelithiasis, etc.

Chromocystoscopy. Observation of kidney function by the cystoscope after subcutaneous injection of colored fluid which is then excreted by the kidneys. The quantity ejected by each ureter is a measure of the relative work done by each kidney.

Chrysoform. Dibromodiiodohexamethylenetetramine. Antiseptic dressing powder.

Clinography. A system of expressing clinical findings by a series of symbols.

Cocadrenine. Trade name for a combination of adrenalin borate and cocain with coca-butter. Used for suppositories.

Colposcope. A tubular instrument with a transparent cap for inspecting the inflated vagina.

Conserves. A term proposed to apply exclusively to articles of food sealed in airtight cans, jars or bottles.

Contratussin. A preparation resembling antitussin. Used in whooping cough.

Convulsion. A preparation of eucalyptus used for treatment of diseases of the respiratory organs.

Copraol. Purified cocoanut oil. Used as base for medicaments.

Coprology. Scientific study of the feces.

Cornutol. A concentrated aseptic preparation of ergot.

Cotargit. Double salt of cotarnine hydrochlorate and ferric chlorid. Hemostatic.

Creolol. Saponified coal-tar creosote. A disinfectant used in ¼ per cent and stronger solutions.

Creosotina. Compound of beechwood creosote, benzoic acid and carbonic acid. Antiseptic.

Crethol. An alkaline, saponaceous disinfectant, a cresylic acid compound. Used in one to five per cent solution.

Crounotherapy. [Gr. Krounos, a spring.] The use of mineral waters for drinking cures.

Culicide. A mosquito exterminator composed of equal parts carbolic acid and gum camphor. It is explosive.

Cuprocitrol. Cupric citrate. Used in ophthalmological practice.

Cutolin. Aluminum biborate. Made up in form of pencil. Styptic, useful in minor hemorrhages.

Cyclodialysis. An operation for glaucoma, establishing communication between the anterior chamber of the eye and the suprachoroidal space.

Cytase. A ferment contained in phagocytes.

Cytoryctes luis. A sporozoan found in the blood of syphilitics.

D

Dechloridation. Suppression of the ingestion of salt.

Deuterotoxin. A toxin which in the scale of variation is medium in its virulency and affinity for antitoxin.

Dialium ferrum. The Brazil ironwood tree, the same as Pao-ferro, q. v.

Diarrhea pancreatica. Thin, profuse evacuations accompanying cysts or paraenchymatous degeneration of the pancreas.

Digalen. Amorphous digitoxin. Put

up in glycerin-water solution, each c.c. of which contains 0.3 mg. of the substance.

Digitalysatum Burger. A digitalis preparation, 1 gm. of which is said to contain 0.7 mg. crude digitoxin.

Disease. Serum d. The symptoms, which may be acute and profound, caused by a second injection of sterile alien serum, the first injection having caused no trouble.

Disease, Still's d. A syndrome of polyarthritis, enlarged spleen and greatly enlarged lymph glands. Probably of infectious origin. Prognosis grave.

Disinfectol. By-product in camphor manufacture; contains camphor, terpene, naphtalin, etc. Used as disinfectant.

Diurol. A combination of lithium benzoate, buchu, triticum, saw palmetto, potassium bicarbonate, etc. Sedative diuretic.

Dourine. A specific blood disease of the horse characterized in the early stages by morbid changes in the genitourinary organs and later by systemic involvement. So-called equine syphilis.

Duotonol. A preparation of lime and soda glycerophosphates.

Dysantigraphia. An inability to write by copying. The result of a lesion in the association path between the word-seeing and word-writing centers.

E

Echinol. Concentrated liquid preparation of echinacea.

Elchina. An elixir of cinchona containing also sodium glycerinophosphate and nux vomica.

Enelectrolysis. The method of removing superfluous hair by first pulling out the hair and then passing the electric needle into the hole left and turning on the current.

Energetenes. Remedial agents stated to be the fresh juices of various plants.

Enesol. Mercury salicylarsenate. Combines the action of mercury and arsenic, the salt being equal in effect to a like quantity of mercuric iodid.

Enterotoxismus. A name proposed for autointoxication of enteric origin and defined as: A morbid condition characterized by the absorption of substances from the gastrointestinal tract which are toxic by virtue of their quantity or quality and which are produced therein by the disintegration of foodstuffs through the perverted and prolonged action of enzymes or the activity of entophytes.

Eosol. Surgical germicid.

Epiploopexy. The same as omentopexy, q. v.

Epirenan. A solution, 1:1000, of the active principle of the suprarenal glands.

Epitoxoid. Toxin units which in a quantity of toxin partially neutralized by antitoxin remain free because of their weak affinity for antitoxin.

Erepsin. A ferment found in the succus entericus of man and animals which transforms hemi-albumose into other bodies.

Ergotherapy. Cure by physical self-effort.

Ethylnarceine hydrochlorat. The same as narcyl, q. v.

Eucain lactate. Used as a local anesthetic, in like manner to eucain.

Eugoform. Acetylated methylenediguaiacol. Used locally as an antiseptic in various skin diseases. **Soluble e.** A 50 per cent solution of engoform in acetone.

Eumydrin. Methyl-atropinium nitrate. White, crystalline, odorless salt. Soluble in water and alcohol. Equal in strength of atropin to atropin sulphate. Claimed to be much less poisonous. Succedaneum for atropin internally and externally. Average dose: 1-64 grain.

Euphagia. The correct manner of partaking of food.

Euporphin. Apomorphin brommethylate. Use same as apomorphin hydrochlorate.

Eusoma. Echinacea compound. A proprietary intestinal disinfectant compound, used also as dressing for affections of the skin.

Euzone. A white, stable, odorless, nonirritant powder. Represents 22 per cent by weight of hydrogen peroxid. Solutions said to possess all the valuable qualities of hydrogen peroxid without being acid. Five per cent euzone equals 1 per cent hydrogen peroxid.

F

Fasciolopsis Buskii. A trematode or fluke found parasitic in the small intestine of man. Very rare in this country, commoner in Asia. Causes intestinal irritation and anemia.

Ferasquin. A preparation of iron, quinin and arsenic.

Fermanas. A preparation of iron, manganese, strychnin and arsenic.

Ferrozone. A ferrous vanadate.

Fetron. Ointment base containing stearic-acid anilid. Consistency between those of lanolin and petrolatum.

Fever Mosquito f. An acute febrile disease which attacks unacclimated subjects in Herzegovina with the onset of the mosquito season. It leaves permanent immunity.

Fibrolysin. A combination of thiosinamin with sodium salicylate. Soluble in water. May be injected subcutaneously or intramuscularly. Used to break down fibrous tissue.

Fistula Eck's. An operation for relief of cirrhosis of the liver. Vascular exclusion of the liver by termino-lateral anastomosis of the portal vein into the vena cava.

Fluid Fralick f. A germicidal fluid for intravenous injection in tuberculosis. The active ingredients are nascent chlorin and ozone.

Fluid, Mitchell's f. A combination of water, sodium chlorid, bromin and hydrochloric acid treated by an electric current. Dose: up to 6 ounces daily. Supposed to exert a curative effect upon pulmonary tuberculosis.

Fluoroform. A gas, CHF_3, used in the form of fluoroform water, 2 per cent solution. Odorless, tasteless, nontoxic. Dose: 1 to 4 drams. Used for whooping cough.

Fomitin. Fluid extract of **fomes cinnamomeus** and **F. igniarius.** Used in affections of the genitourinary tract. Dose: 1 to 4 tablespoonfuls.

Forman. Chlormethyl menthyl ether. Decomposes through moisture of the air into formic aldehyde, menthol and hydrochloric acid.

Formin oxymethylsulphonate. The same as thial, q. v.

Formolid. An antiseptic solution containing ¼ per cent formaldehyde, eucalyptol, alcohol, etc.

Fucol. A preparation made from algae containing iodin. Used as a vehicle for exhibiting phosphorus, creosote, iodin, etc.

G

Garantose. A trade name for saccharin.

Gastroxynsis. The condition in which mental overexertion, etc., has led to the secretion of an abnormally large quantity of gastric juice.

Genoform. An antirheumatic and uric acid solvent.

Glossina palpitans. The tsetse fly which introduces a trypanasome into the blood of various animals.

Griserin. The same as loretin, q. v.

Guaiodol. Compound of guaiacol, iodin and bismuth. Antiseptic dressing powder, styptic and astringent.

Guayarsin. A compound of guaiacol and arsenic.

H

Haeman. Preparation of iron-sulphocyanate used as tonic.

Hemisine. Preparation of the active principle of the suprarenal glands.

Hemoantitoxin. Said to be the same as Maragliano's antitoxin for tuberculosis. Dose: 4 tablespoonfuls a day.

Hemonephrosis or Hematonephrosis. The presence of blood in the pelvis of the kidney.

Hepar. A combination of cascara, aloin, podophyllin, etc., in tablet form.

Hepatargy. [Gr. argia, inactivity.] Hepatic intoxication. The form of autointoxication resulting from defective elaboration of the various substances which the liver produces or converts.

Hepatitis sequestrans. That form of inflammation of the liver in which retained bile in combination with the action of bacteria forms necrosis and disintegration of the tissues.

Heterotoxis. Poisoning by a toxin directly introduced into the organism, the opposite of autotoxis or autointoxication.

Hetralin. A urinary antiseptic. Dose: 15 to 25 grains a day.

Hexamethylene-tetramine or Hexamethylenamine. A urinary disinfectant; the same as urotropin, aminoform, cystamine, cystogen, formin, ammonio-formaldehyde, etc.

Hexamine. Trade name of hexamethylene tetramine.

Histosan. Guaiacol-albumin compound. Used in diseases of respiratory tract. Dose: 1 to 4 drams.

Humidify. To render moist. Especially used in describing the function of the nasal mucous membrane.

Hydnocarpus. A tree found in India from the seeds of which is expressed an oil allied to Chaulmoogra oil. In doses of 15 minims to 2 drams it is prescribed for various skin diseases.

Hydrargyrin. Mercurial ointment with lanum base.

Hydrargyrum anilinicum. A mercurial salt resulting from an admixture of anilin and sublimate.

Hydroacetyl dioxid. Produced by adding benzoylacetyl-peroxid to water. An antiseptic.

I

Ichthoidine. A fluid containing ichthyol, iodine, glycerite of hydrastis, boroglyceride, etc. Local application in chronic metritis, etc.

Icterus, Akathectic I. [Gr. akathexis, a failure of retention.] Jaundice caused by functional disturbances in the liver cells with or without demonstrable anatomic alterations. Diffusion icterus.

Ictometer. An instrument applied over the chest wall to estimate heart action.

Insanoid. Simulating or resembling insanity.

Intestin. Intestinal antiseptic containing bismuth, naphtalin, etc. Dose: 7 to 15 grains.

Iodgelatin. Compound of gelatin, iodin and potassium iodid with hypophosphites. Tonic. Dose: teaspoonful.

Ioterpin. Compound of iodin and terpin hydrate. Antiseptic dressing powder or as ointment.

Iothion. An oily fluid containing 70 per cent iodine. Insoluble in water, soluble in oils, alcohol, etc. Used mixed with lanolin, vaselin, etc., for inunction treatment of syphilis, etc.

Isobodies. Antibodies which are active for the tissue constituents of other animals of the same species to which the originating animal belongs.

Isoform. Antiseptic dressing powder, or used as antiseptic paste or solution.

Isoprecipitin. A precipitin which proves active against the serum of other animals of the same species to which the originating animal belongs.

J

Jatrevin. Condensation product of menthol-camphor and isobutyl-phenol. Used in spray of 2 to 5 per cent solutions in diseases of respiratory passages.

K

Kama Kosin. Mixture containing active constituents of Kamala and Kousso. Anthelmintic for tapeworm.

Kju. A fibrous vegetable substance in the form of a cylinder which when wet adheres to the skin and if lighted burns slowly, giving mild irritation. Used in Japan.

Kreoformin. A condensation product of creosote and formic aldehyde.

L

Lactodensimeter. The same as lactometer, an accurately gauged hydrometer for showing the specific gravity of milk.

Lactoserum. A serum which contains a precipitin which throws down the casein of milk from the same species as that used for injection.

Lecithan. A preparation of lecithin.

Leprolin. A preparation of the toxin of the bacillus of leprosy. Used in the treatment of leprosy.

Levurargyre. [Fr. levure, yeast.] A mercurial nucleo-proteid extracted from brewer's yeast grown in a wash containing bichlorid of mercury. Used for treating cutaneous manifestations of syphilis.

Levurinose. A preparation of beer yeast. Dose: 1 to 4 teaspoonfuls.

Liquor diastos. An artificial digestant containing pepsin, diastase, trypsin, nitrohydrochloric acid, nux vomica, etc.

Liver, Feuerstein l. A smooth cirrhosis of the liver found particularly in children as the result of congenital lues.

Loretin. Meta-iodo-ortho-oxy-chinolin-ana-sulphuric acid. A yellow, inodorous, insoluble powder containing 36 per cent iodin, a substitute for iodoform. Used externally and internally.

Lucotherapy. [L. lux, light.] Healing by the application of light.

Lysargine. Colloidal silver containing 60 per cent of the metal. Antiseptic.

M

Macrocytase. The cytase contained in the macrophages.

Macrophage. One of the large phagocytes, including the large lymphocytes, endothelial cells, ameboid connective tissue cells and others.

Mal de Caderas. A tropical disease caused by infection with a variety of trypanosoma, a genus of sporozoa.

Maladie du coït. So-called equine syphilis or dourine, q. v.

Maloplasty. Plastic surgery upon the cheek.

Mangasol. Manganese chlorophenolsulphonate. Internal antiseptic. Dose: 10 to 30 grains.

Maretin. Carbaminic-acid-meta-tolylhydrazid. A white, tasteless powder. Antipyretic and antineuralgic. Said to have no untoward effects. Dose: 3 to 7 grains. Effect is prolonged.

Meatoscopy. Cystoscopic inspection of the ureteric orifices.

Menstruatio precox. Premature menstruation. Periodical genital hemorrhage occurring in infancy or long before the usual age of puberty.

Mesenteriolum. A small mesentery such as is occasionally attached to diverticula of the intestine.

Metapsychics. A term to characterize the subconscious and occult phenomena, those beyond the realm of consciousness.

Methyl-aspirin. The same as methylrhodin. Used the same as the salicylates.

Microcytase. The cytase contained in the microphages.

Microgastry. Undersize of the stomach, retention of the infantile type.

Microphages. One of the polymorphonuclear leucocytes, the smaller phagocytes.

Miopragia. [Gr. meion, less; prasso, to do.] Lessening of the ability to function.

Misocainia. [Gr. misein, to hate; kainos, new.] The inclination to combat new ideas.

Misoneismus. [Gr. neios, new.] Obstinate opposition to innovations.

M. L. D. Minimum lethal dose. A term used by makers of therapeutic sera.

Monilia candida. A yeast organism cultivated from intestinal contents, probably identical with saccharomyces albicans or thrush.

Monothermia. The condition in which the patient's temperature remains the same morning and evening.

Mucol. A salicylic acid preparation used in infectious diseases of mouth and larynx.

Mulyptol. A fluid preparation of eucalyptol and other derivatives of Australian eucalyptus.

Myatonia. A deficiency or absence of muscular tone observed especially in infants, affecting various parts or the entire voluntary muscular system.

Mycodermine. An extract of yeast.

Myelomatosis. Multiple myeloma. A diffuse new growth primarily involving the bone marrow and arising in various bones.

Myogen. A nutrient albumin derived from blood serum.

N

Naphtosalicin. A disinfectant compound of naphtol and salicylic acid.

Narcosomania. The same as narcomania, the insane desire for the effect produced by narcotics.

Narcyl. Ethylnarcein hydrochlorate. A general analgesic. Dose: 1 grain a day, hypodermatically 1-6 to 1-3 grain.

Natrozone. A compound of hydrogen dioxid.

Neoquinin. Quinin glycerinophosphate.

Nephritis, Hypogenetic n. Kidney disease which arises from an unusual strain upon kidneys congenitally underdeveloped.

Neurarchy. A term indicating the supreme rule exercised over the body by the cerebro-spinal system.

Neuronal. Bromodiethylacetamid. Gray crystalline powder with taste of menthol, slightly soluble in water. Dose: 7 to 15 grains. A hypnotic said to be harmless.

Neuronidia. A liquid containing veronal 4 grains to each dessertspoonful.

Neuronophages. Mononuclear phagocytes which in old age form a zone around the nerve ganglion cells and are thought to cause atrophy of the latter.

Nioform. The same as vioform, q. v.

Norgine. Calcium tangate prepared from sea tang.

Nutrescine. A hypothetical substance necessary for the nutrition of the cell and which is split off from the molecule of bioplasmine, q. v.

O

Oidium coccidioides. A fungus which develops spherical bodies with endosporulation in the tissues, but on media has a mould-like growth. Most tissues of the body may be invaded. The clinical and anatomic results of infection greatly resemble tuberculosis.

Olan. Paraffin ointment base, giving emulsion when mixed with water.

Oligoposy. [Gr. posis, a drinking.] The condition of disturbance which arises from not drinking enough fluids.

Ombrophore. An apparatus which effects the application of a douche bath with water saturated with carbon dioxid.

Omentopexy. The operation of fixing the omentum to the anterior abdominal wall and so establishing anastomotic channels between the portal system and that of the vena cava.

Onyalai. A West African disease. It is characterized by the appearance of hemorrhagic vesicles on the buccal mucous membrane which last about ten days and are not accompanied by fever.

Ophthalmol. An oil instilled in the eye for treatment of granulated lids.

Orthoroentgenography. A word recommended in place of orthodiagraphy, the use of the orthodiagraph, q. v.

Osmology. The knowledge concerning the physical conditions of and in the body fluids.

Osmosum. A preparation of aluminum silicate and glycerin used externally as antiphlogstic, etc.

Oxychlorine. Tetra-borate of sodium and potassium with oxychloride of boron. A light yellowish powder, soluble in water. Used as powder or in solution for wound disinfecting and dressing.

Oxydasine. Preparation of vanadic acid and glycerin.

P

Pao-ferro. The Brazil ironwood tree, the tincture of the inner bark of which is said to have remarkable antidiabetic properties.

Paracholia. Diffusion icterus caused by functional disturbances in the liver cells. The same as akathectic icterus, q. v.

Paraiodanisol. The same as isoform, q. v.

Paralysis, Bernhardt's p. Disturbance caused by disease of the external cutaneous nerve of the thigh. There is pain and hypesthesia in the outer surface of thigh.

Paranephrin. A preparation of the active principle of the suprarenal glands. Used in 1:1000 solution. Local and general hemostatic.

Parapedesis. [Gr. para, beyond; pedan, to pass or ooze.] An oozing through, especially of the bile-pigment into the blood-capillaries instead of the bile-capillaries as a result of pathologic changes in the liver-cells.

Percutilan. An ointment base.

Perhydrol. A 30 per cent, by weight, of hydrogen peroxid.

Perseveration. A perseverance in the utterance of one word or of one idea in response to raised questions.

Petrogen. A bland preparation of mineral oil which readily forms an emulsion with water and serves as a vehicle for various external and internal remedies.

Petro-kreosote. A combination of petrolatum, beechwood creosote, gentian and sherry wine. Tonic in respiratory diseases.

Phagokaryosis. The phenomenon of phagocytosis carried out by the cell nucleus which normally does not take part in phagocytic action. It can be induced by injections of lecithin.

Phagolysis. Solution, partial or complete, of phagocytes.

Plasmin. Cell juice which has been expressed from some micro-organisms.

Phenalin. A preparation of phenolphtalein in talbet form. Cathartic.

Phenomenon of Koch. The quick succumbing of tuberculous animals when inoculated intraperitoneally with a fresh culture of tubercle bacilli. The resulting exudate contains almost exclusively lymphocytes.

Phorxal. Organic iron preparation containing phosphorus.

Phthisopyrine. Preparation containing aspirin, camphoric acid and arsenous acid used in tuberculosis as antipyretic.

Phytin. Calcium and magnesium anhydroxymethylene diphosphate. Dose 7 grains.

Phytoprecipitin. A precipitin produced by immunization with albuminous substances of plant origin.

Piezometer. An instrument for measuring resistances whether of the overlying muscles and walls or of the underlying object, such as an abdominal tumor.

Plasmeba. The parasite of dengue, which is a sporozoan and was found first in blood plasma.

Pneumin. Methylenecreosote. Used in tuberculosis.

Precipitogen. Any albuminous substance immunization with which will cause the formation of a specific precipitating serum.

Preserves. A term proposed to apply to foodstuffs preserved from decomposition by any method, salting, freezing, etc.

Prevalidin. Camphor ointment for inunction. Used in phthisis.

Proferrin. Iron nucleoproteid. A reddish-brown powder insoluble in water and acid solutions. Contains 10 per cent organic iron. Nonastringent. Dose: 5 to 10 grains.

Progeria. [Gr. geron, old.] Retarded development, combined with premature old age.

Prostatodynia. Pain in the prostate gland.

Prototoxin. A toxin which in the scale of variation is the most virulent and has the greatest affinity for antitoxin.

Protoxoids. Toxoids which have the greatest affinity for antitoxin.

Psomophagic. [Gr. psomos, a morsel.] Eating in small pieces, chewing thoroughly.

Psychasthenia. Psychic forms of neurasthenia.

Pyrenol. Combination of salicylic and benzoic acids with thymol and a sodium salt. White, soluble powder with aromatic odor. Dose: 60 grains daily. Used for rheumatism and diseases of the respiratory tract.

Pyroligneine. A proprietary antiseptic wound dressing.

Q

Quartonol. A preparation of lime, soda, quinin and strychnin glycerophosphates.

Quinimel. A nonmedicinal adjuvant for disguising the taste of bitter drugs.

R

Rachicentesis. Puncture of the spinal canal. Lumbar puncture.

Rectoromanoscope. An instrument for introducing a rectal tube for inspection or treatment high into the bowel.

Reflex, Kocher's r. Compression of the testicle causes in the normal individual contraction of the abdominal muscle on the same side.

Renatone. A proprietary diuretic and urinary disinfectant, said to contain digitalis, triticum, buchu, etc.

Rexotan. Methylene-tannin-urea. Intestinal antiseptic. For treatment of intestinal catarrh.

Rhomnol. A nucleinic acid obtained from the thymus gland and employed like lecithin or glycerinophosphates.

Ringolin. Combination of cod liver oil and glycerin with zinc oxid and balsam Peru. Used as a vehicle for applying medicines to the skin.

Roentgenize. A verb signifying use of the Roentgen rays.

Roentgenography. Photography by the Roentgen rays.

Roentgenology. The study or science of the Roentgen rays.

Roentgenoscopy. Observation made by the means of the Roentgen rays.

Roentgenotherapy. Treatment by means of the Roentgen rays.

Ruscol. Compound of bismuth and birch tar used in treating eczema, erysipelas, etc.

S

Salit. Borneol salicylate. Used by inunction or painting over affected part in cases of rheumatism, neuralgia, etc.

Salithia. A combination of magnesium sulphate, lithium and colchinine in effervescent form.

Salusol. A distillate of the alkyl acetates and antiseptic volatile oils, forming a compound spirit of acetic ether. External and internal use as antiseptic, germicide and astringent.

Salvin. Compound of ethereal silicaceratin. Used in treating skin affections.

Saparaform. A paraform soap used as an antiseptic. It evolves formaldehyd.

Scarlatinoid, Metadiphtheric s. .The erythema which sometimes develops with a syndrome resembling that of scarlet fever in a patient convalescing from diphtheria.

Scolecoiditis. [Gr. skolex, worm.] Appendicitis.

Seda-derma. A sedative ointment containing ichthyol, zinc oxid, resorcin, etc.

Sedatole. A proprietary remedy for respiratory affections, containing expectorants and heroin 1-24 grain to each dram.

Septotome. A cutting instrument used as substitute for the knife or scissors in operating on the nasal septum.

Serum, Anticrotalic s. [Crotalus, a genus of poisonous serpents, including rattlesnakes.] Serum which combats the bite of rattlesnakes.

Serum, Anti-ophidic s. [Ophidia, the order of reptiles, including serpents.] Serum which combats the poison of snakes.

Sextonol. A preparation of lime, soda, iron, manganese, quinin and strychnin glycerophosphates.

Sialangitis pancreatica. Inflammation of the pancreatic ducts.

Sialorrhea pancreatica. The spitting or vomiting of large quantities of fluid resembling saliva or pancreatic juice, sometimes accompanying pancreatic disease.

Siderosis, Hepatic s. Iron-liver. A pathologic condition in which abnormal quantities of iron are stored in the liver. The organ may present at autopsy typical changes in appearance, but the size and consistency are not altered.

Sign, Combined plantar s. The simultaneous abolition of the cortical plantar reflex (flexion reflex) and the spinal plantar reflex (fascia lata reflex). Occurs in hysteria.

Silberol. Silver sulphocarbolate. Said to be a powerful antiseptic. Used for treatment of gonorrhea and in ophthalmic practice.

Silin. Hexamethlenetetramine citrosilicate. Used in combination with alkalies in uric acid diathesis.

Sodium perborate. A powder obtained by the action of boracic acid on sodium peroxid. When the powder is dissolved in water chemically pure peroxid of hydrogen is generated.

Sodium phenylpropiolate. Remedy used in weak solutions for inhalation in tuberculosis.

Sodium sulphobenzoate. Compound prepared from sulphocarbolate and formate of sodium. Urinary antiseptic. Dose: 15 to 30 grains.

Somnalgesine. Amidoacetdiphenyldimethyloxypyrazolon. Antipyretic analgesic and sedative. Dose: 1 to 5 grains.

Sore, Madagascar s. Phagedenic ulcers occurring in tropical countries, probably identical with the former hospital gangrene.

Spirocheta pallida. A form of spiral bacteria found in syphilitic lesions.

Splanchotribe. An instrument, similar to the angiotribe, for crushing the intestine or appendix and so obliterating its lumen.

Stagnin. Substance obtained from spleen of horses. A hemostatic.

Streptothricosis. Infection with some variety of streptothrix.

Succinic peroxid. The same as alphozone, q. v.

Syntoxoid. A hypothetical toxoid which has affinity for antitoxin exactly equal to that of toxin.

T

Tachyphagia. Hasty eating.

Tannobromin. Substance obtained by the action of formaldehyd on dibromtannin.

Tenontoplasty. The same as tenoplasty. Plastic surgery on the tendons.

Test, Peroxid of hydrogen t. (for blood). A 20 per cent solution of H_2O_2 added to any fluid containing blood even in great dilution causes colorless bubbles to rise up in foam. Shows occult hemorrhage in stomach contents, etc.

Tetanolysin. The hemolytic toxin of the tetanus bacillus.

Tetanus paradoxus. The variety of cephalic or hydrophobic tetanus in which there is trismus combined with paralysis of the facial or other cranial nerves.

Thamuria. [Gr. thama, often.] Frequency of urination, differentiated from polyuria.

Theophyllin-sodium. A preparation from the alkaloid of tea. Dose: 7 grains.

Thermic inversion. The condition in which the patient's temperature reaches its maximum in the morning.

Thial. Formin oxymethylsulphonate. Antiseptic and vulnerary in weak solution.

Thiodine. A combination of ichthyol, iodine, hydrastine, glycerin, etc. Used in the form of suppositories for treatment of certain gynecologic affections.

Thymalka. An alkaline antiseptic solution containing sodium borate, thymol, eucalyptol, etc. Used for disinfecting mouth, throat, etc.

Thymiodide. A proprietary antiseptic surgical dressing, odorless and nonpoisonous.

Thymoloform. A condensation product of formaldehyde and thymol which forms a yellowish tasteless powder, proposed as a substitute for iodoform.

Thymol-trichloracetate. Caustic antiseptic for ulcers and wounds.

Thyreoidectin. A preparation of the blood of animals from which the thyroid gland has been removed. Used in treatment of exophthalmic goitre.

Thyroidectomized. A term applied to animals from whom the thyroid gland has been removed to develop desired qualities in their blood and milk.

Tonsil, Submerged t. A tonsil which in repose is hidden behind the faucial pillars, which may themselves be hypertrophied. By gagging the tonsil may usually be made to protrude.

Torula of Pasteur. A micro-organism closely allied to the yeast fungus and which is found in meconium.

Tot. Mixture of isonaphtol benzoylbetanaphtol and abrastol. Internal antiseptic in gastric affections.

Toxin, Normal t. The standard of toxin strength: 0.01 c.c. of it will kill a guinea pig weighing 250 grams in four days.

Toxoid. A toxin in which a loss of toxicity has occurred through alteration or disappearance of a portion of the toxophore groups.

Toxon. A constituent of diphtheria bouillon which causes other phenomena than the acute symptoms.

Triferrol. A liquid preparation of triferrin.

Tritoxin. A toxin which in the scale of variation is the weakest in its virulency and affinity for antitoxin.

Trygase. A preparation of yeast.

Turicin. Compound of tannin and glutonin. Anti-diarrheal in acute intestinal catarrh.

U

Ungrol. A glycerin-gelatin sublamin preparation used as prophylactic for gonorrhea and syphilis.

Uriform. A proprietary urinary disinfectant said to contain hexamethylenetetramine.

Uritone. A trade name for hexamethylenetetramine.

Urocol. Compound of urea quinate and colchicin. For treatment of gout.

Urol. Urea quinate. A remedy used in gout.

Uron. A proprietary diuretic and genitourinary antiseptic and sedative.

Uropural. Compound of uva ursi, salol, aspirin, hexamethylenetetramine, etc. Urinary antiseptic and sedative.

Urosanol. Protargol-gelatin preparation for urethritis, etc.

Urotropin, New u. Urotropin methylene citrate. The same as helmitol, q. v.

Uterol. A combination of black haw, aletris, hydrastis, somnos, etc. Antispasmodic and sedative for uterine disorders.

V

Vasenol. Emulsifiable ointment base. A vehicle for medication in skin affections.

Y

Yeast, Encapsulated y. A micro-organism obtained from intestinal contents. It is encircled by a gelatinous capsule.

Yeast, Red y. A micro-organism which has been found in meconium and which is often present in the air. On artificial media it forms colonies of a scarlet color.

Z

Zerodone. An apparatus for cooling the rectum by means of maintaining a circulation of liquid at low temperature.

Zinc dioxid. The same as dermogen, q. v.

Zooprecipitin. A precipitin obatined by immunization with albuminous substances of animal origin.

Zymeoid. A double borate salt containing 50 per cent oxygen. White, crystalline, tasteless. Gastrointestinal antiferment.

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